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Vol. XXIII, No. 3 MARCH, 1934

JOURNAL OF THE AMERICAN PHARMACEUTICAL ASSOCIATION

TRADE MARK

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THE 82nd ANNUAL MEETING OF THE AMERICAN PHARMACEUTICAL ASSOCIATION WILL BE HELD IN WASHINGTON, D. C., DURING WEEK OF MAY 7, 1934.

The 1934 Meetings of the American Association of Colleges of Pharmacy, the National Association of Boards of Pharmacy, Conference of Pharmaceutical Association Secretaries, of the Pharmaceutical Law Enforcement Officials and the Plant Science Seminar will also be held in Washington.

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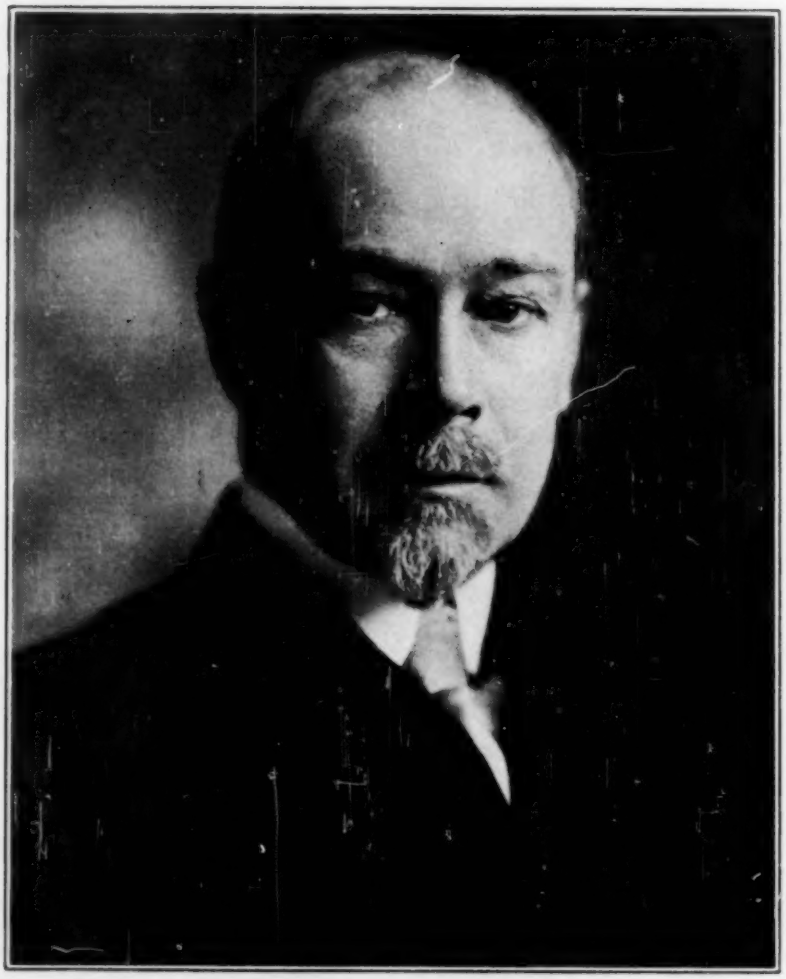
The reprint contains much information which should be of practical value for increasing prescription practice; wholesalers and manufacturers will want them; schools of pharmacy will find them of value for their students.

Exhibit of the College of Pharmacy of the University of Minnesota at the Drug Exposition of the Northwest Drug Bureau in the Municipal Auditorium, Minneapolis, February 13 to 16, 1934, on the occasion of the Golden Anniversary of the Minnesota Pharmaceutical Association.



FREDERICK J. WULLING.

JOURNAL OF THE AMERICAN PHARMACEUTICAL ASSOCIATION

VOL. XXIII MARCH, 1934 No. 3

FREDERICK J. WULLING.

Frederick John Wulling, president of the AMERICAN PHARMACEUTICAL ASSOCIATION, 1916–1917, has been dean and member of the faculty of the College of Pharmacy of the University of Minnesota for more than forty years. He was born in Brooklyn, N. Y., December 24, 1866, the son of John J. and Louise C. (Munz) Wulling. In 1883, he graduated from Carlstadt, N. J., high school; after completing a course of study in a business college, he matriculated at Columbia University College of Pharmacy and graduated in 1887. Following graduation, the young man was named Associate Editor of the *Pharmaceutical Record*, in which capacity he served until 1891, when he accepted place as member of the faculty of Brooklyn College of Pharmacy.

In 1892, Professor Wulling was elected member of the faculty and dean of the College of Pharmacy, University of Minnesota, and when, under his direction, the Medicinal Plant Garden was established he was named director. During the War this garden contributed a great service by supplying standardized Tincture of Digitalis. While an outstanding purpose of the garden is to coöperate with medicine and pharmacy in the educational promotions of the University and for the student bodies of these divisions, Dr. Wulling brings its message to the citizens of Minnesota by acquainting them with native useful as well as dangerous or poisonous plants. The University outlook and purpose is presented in radio and other addresses by the Dean for general information of the public in which the importance of professional pharmacy is stressed.

Among the honors and degrees which Professor Wulling has received are: Pharm.D. and LL.B., University of Minnesota; Ph.M., Philadelphia College of Pharmacy and Science; honorary Sc.D., Columbia University. He was trustee of the U. S. Pharmacopœial Convention 1920–1930; president of the American Conference of Pharmaceutical Faculties, 1914–1915; chairman of the Minnesota Academy of Sciences, 1910; is director of the Minneapolis Society of Fine Arts; fellow of the American Association for the Advancement of Sciences; and various literary

and social clubs; honorary member of New Jersey Pharmaceutical Association; member of Minnesota Pharmaceutical Association; and presides over the session of its scientific and practical pharmacy section at its meeting with Northwestern Branch A. PH. A.

He is author of "Evolution of Botany," 1891; "Medical and Pharmaceutical Chemistry," 1894; "Chemistry of the Carbon Compounds," 1900; "Course in Law," 1908.

Dr. Wulling married Miss Lucille Truth Gissel, of Brooklyn, in 1897; they have one son, Emerson G. Wulling. This sketch has been prompted by a service as dean of the pharmacy faculty of the University of Minnesota, covering a period of more than four decades.

SIR HENRY WELLCOME, REMINGTON MEDALIST FOR 1934.

Secretary Hugo H. Schaefer, on March 16th, announced the vote of Remington Honor Medal Committee, naming Sir Henry Wellcome as Remington Medalist for 1934. The recipient has been a member of the AMERICAN PHARMACEUTICAL ASSOCIATION since 1875, a sketch is printed on page 573 of the July JOURNAL, 1925; see also January number, 1932, page 88; July, pages 644, 647.

Mr. Wellcome was knighted by King George and has been elected fellow of the Royal College of Surgeons. He is the second person, not holding a medical degree, aside from members of the Royal Family, thus honored; the other recipient was Field Marshall Lord Roberts.

His monumental sanitary work in various parts of the world is referred to at this time, because his report to the Secretary of War resulted in a greatly increased Government support of the methods and operations of General Gorgas in Panama. He is director of the Gorgas Memorial Institute of Tropical and Preventive Medicine, Washington, which operates scientific laboratories at Panama for research relating to causes and prevention of tropical diseases.

Sir Henry is a native of Wisconsin and a graduate of the Philadelphia College of Pharmacy. The late Dr. Frederick B. Power[1] was director of the Wellcome Chemical Research Laboratories in London.

On account of the lateness of publication the sketch of Sir Henry and outline of his activities will have to be deferred to the April issue of the JOURNAL.

LOCAL COMMITTEES FOR THE 82ND ANNUAL MEETING OF THE AMERICAN PHARMACEUTICAL ASSOCIATION IN WASHINGTON, D. C., WEEK OF MAY 7TH.

Headquarters—Hotel Shoreham.

Local Secretary, Frank A. Delgado, 1620 Fuller St., N. W., Washington, D. C.

Convention Committee: Paul Pearson, *Chairman;* F. B. Campbell, M. G. Goldstein, G. W. Mathews, B. A. Smyser, J. G. Biggs. *Treasurer,* T. A. Moskey; *Secretary,* A. F. Gorsuch.

Chairman of Sub-Committees: *Womens,* Mrs. T. A. Moskey, Mrs. T. B. Campbell. *Entertainment,* W. P. Herbst. *Dedication,* S. L. Hilton.

Auxiliary State Committees: *Delaware,* Thomas S. Smith, *Chairman;* Thomas Donaldson, J. W. Wise, Albert Dougherty, A. S. Williams. *Maryland,* S. Y. Harris, *Chairman;* R. E. L. Williamson, L. V. Johnson, Simon Solomon, F. L. Black. *Virginia,* A. L. I. Winne, *Chairman;* N. Guy Miller, H. C. Littlejohn, E. P. Berwyn, W. G. Crockett. *West Virginia,* J. Lester Hayman, *Chairman;* C. V. Selby, G. O. Young, R. B. Cook, E. K. Hoge.

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[1] For sketch of Dr. Frederick Power—see June JOURNAL, 1922, page 403.

EDITORIAL

E. G. EBERLE, EDITOR 2215 Constitution Ave., WASHINGTON, D. C.

A CORDIAL WELCOME.

THE time and place for the 1934 meeting of the AMERICAN PHARMACEUTICAL ASSOCIATION—Washington, May 7th to 12th—were selected to accord with the plans for dedicating the Headquarters Building. The occupancy of this building which with other structures that may later be erected on the site will be known as the American Institute of Pharmacy, is one of the most important events in the long history of the ASSOCIATION and marks the successful completion of the most extensive and far-reaching effort the ASSOCIATION has undertaken. The site, the building and the surroundings are beyond the expectations even of those who have been most active in the undertaking, and it is difficult to forecast the helpful influence which the institute will exert in the years to come. American pharmacy now occupies its home and will be equipped to more effectively carry forward those activities which contribute to a stronger profession and to a better pharmaceutical service for the public.

Every branch of pharmacy has had a part in this movement and thousands of individuals and organizations have contributed of their time and thought and money. Its success is a distinct credit to the profession and to the industry, and is a striking example of what can be accomplished through coöperation. With such a splendid foundation and equipment, even greater results may be expected and pharmacy should take its rightful place among the professions which safeguard the public health.

The dedication exercises which will be held at the building on Wednesday morning, May ninth, will be simple and impressive. With this exception, the usual program for the meeting will be carried out at the Shoreham Hotel which has been selected as the headquarters.

The National Conference on Pharmaceutical Research will hold its sessions on Saturday, the fifth, in the afternoon and evening. The American Association of Colleges of Pharmacy and the National Association of Boards of Pharmacy will meet Monday and Tuesday. The joint banquet will be given on Tuesday evening and the regular program of the AMERICAN PHARMACEUTICAL ASSOCIATION will occupy the remainder of the week, closing Friday evening. Saturday will be devoted to a sight-seeing trip around Washington, Arlington, Alexandria and Mt. Vernon.

The members of the District of Columbia Pharmaceutical Association will be the hosts. Ample accommodations are available and a splendid program of entertainment is provided. The Capital City is at its best at this time and all the points of interest will be open.

A cordial invitation is extended to our members, to every one who contributed to the Headquarters Building, and others interested in the progress of Pharmacy, to attend the meeting and particularly the dedication on May ninth. It is impossible to send a special invitation to every one and our earnest desire is that no one should fail to understand that the invitation is all-inclusive of those interested.—ROBERT L. SWAIN, *President.*

THE NRA MAY STRESS THE DRUGGISTS' RESPONSIBILITIES AND POINT TO THE WAY FOR IMPROVING DRUG STORE PRACTICE.

THE codes which apply to the administration of the NRA have impressed the fact that greater efforts must be made to bring pharmacy forward in the average drug store and more careful consideration must be given to the sales in a drug store and the means of promoting them. A very important question for druggists is associated with obtaining their share of the spending power of the public, but to derive it from sales that do not belittle them by selection and quality of side-lines. The drug store has had the prestige of pharmacy and this may be obscured if not lost, if too much stress is placed on price, by reducing standard products to uneconomic levels, selling varied sundries and offering unwarranted premiums to attract patronage. The public has always looked to the druggist for quality, accuracy and service—a valuation that may be lowered if a majority of drug stocks closely resemble the merchandise lines of non-related stores and "cut" prices emphasize that there is no difference in their kind and quality.

The drug store's foundation, pharmacy, has always given the former a higher standing, but continued under-valuation of the foundation and a tendency to have drug stores resemble merchandise emporiums is molding public opinion accordingly. The code relating to the retail drug industry has brought druggists, proprietors and clerks, face to face with the possibilities of lessened prestige. The public has had a large part in the development of the complex drug store. The following lines by a layman are quoted: "I like drug stores. It's reassuring to know that if you run out of anything, from aspirin to birthday greetings you need only to make a short promenade to the neighborhood pharmaceutical establishment." . . . "So let there be drug stores. They're not only soothing; they're even necessary."

THE VALUE OF RESPONSIBILITY.

The matter of adequate charge for time is sometimes overlooked in prescription practice, and insufficient thought is frequently given to the responsibilities pharmacists assume in connection with their activities. In these NRA days, perhaps more than ever before, the pharmacist must concern himself with actual net profit. Liberty is taken in quoting from an article by J. C. Peacock, presented before the Section on Commercial Interests, A. PH. A., in 1917, which is applicable.

"The responsibility of the pharmacist is of peculiar form, if for no other reason than that it is a by-product of his work; consequently, the more work, the more responsibility. Responsibility is a condition of several phases; one phase of it is its part of or its presence in the mentality of the compounding; thus it is proportionately entitled to recognition, if the manipulation itself is worthy of notice; it is, therefore, not only service, but profound service; as service, it should be figured as expense; and as expense, it should be considered in the fixed charges and provided for accordingly." The author submitted the following:

> "That the responsibility of the pharmacist is part of the service which he renders, in truth, the most profound part.
>
> "That responsibility seems to have been generally neglected as a source of revenue.
>
> "That it is thereby shown to have been underestimated by many.

"That its possibilities should be understood and accordingly appreciated by all pharmacists, that it may rise in their own esteem to that plane where it belongs.

"That it should be capitalized at a value which prohibits it from being given away, while the twine around the bundle is charged to the expense account.

"That each pharmacist must do this for himself.

"That now is the golden opportunity to correct this waste.

"That suggestions and experiences be given toward the solution of this problem for the common good."

THE TREND OF PRESCRIBING IN GREAT BRITAIN.

THE *Pharmaceutical Journal* (England) comments editorially on the trend of prescribing in Great Britain and makes references to the surveys made in the United States. A few points of interest for American pharmacists can be gleaned from the editorial which summarizes three reports, one is a study of 40,000 prescriptions, the ingredients of which are to a limited extent restricted by regulations which obtain in dispensing under the National Health Insurance Acts; one is an analysis made in 1894 by W. Martindale of 12,000 prescriptions; another, by B. Cockburn, in 1913, of 1000 London prescriptions.

Several deductions are of general interest; considering the first ten drugs and preparations of the three lists, it is found by the editor that the prescribing of quinine sulphate, potassium bicarbonate and aromatic spirit of ammonia has declined; sodium bicarbonate, tincture of nux vomica and ammonium carbonate have retained their places during the last forty years. Potassium bromide shows a decline and the editor comments by questioning: "Does this mean that bromides are being replaced by other sedatives, or is it an indication that in spite of psychopathists' warnings mankind is less in need of sedatives to-day than in quieter times of last century?" Another comment is of interest, namely, "that acetanilid, on which numerous adverse comments have been made, is prescribed with greater frequency than the newer analgesic"—(the reference applies to aspirin).

STATE LEGISLATION SUPPORTING NRA CODES.

REFERENCE was made in the February JOURNAL to a "model" State industrial recovery act which has been submitted to governors. Acting on the suggestion of Administrator Hugh S. Johnson, State aid to the Federal Government in giving legislative force to NRA agreements as they apply particularly to intrastate industry and business is represented in measures by the legislatures of West Virginia and New Jersey. The West Virginia act signed by Governor Krump places the police power behind code enforcement; the form follows the plan of Administrator Johnson.

Two measures are under way in the New Jersey legislative bodies. Assessment of industry to meet the cost of State Code enforcement with power in the State code authority to sue delinquents is the original purpose of the first measure; the second bill provides for a State appropriation to maintain the State recovery administration. State authorities are denied the power to modify NRA codes, under a provision of the first bill. Another provision requires the State recovery administration to permit an industry to convert from a state code to an NRA code, where a majority of the industry—majority as to number and as to volume of business—shall so elect.

SCIENTIFIC SECTION

BOARD OF REVIEW OF PAPERS.—*Chairman*, L. W. Rowe, George D. Beal, F. F. Berg, C. O. Lee, E. V. Lynn, John C. Krantz, Jr., Heber W. Youngken.

ABSORPTION OF VITAMIN D FROM THE SKIN.*

BY FLORIN J. AMRHEIN.

HISTORICAL INTRODUCTION.

For many years the workers in the field of nutrition have recognized the fact that certain food factors were responsible for many changes that occur in the human body. Many experiments were conducted with various food materials. It was found that pure carbohydrates, pure proteins, pure fats and pure mineral salts were not sufficient to maintain proper body needs and that the presence of other substances in food was apparently necessary.

To Mellanby (1) belongs the credit of the discovery of the specific antirachitic factor, now known as vitamin D. Mellanby, in his reports of 1918 and 1919, gave to the world the first accounts of experimental rickets developed in animals. He used the dog and he showed that rickets could be cured by dietary means.

Hess and Unger (2) in 1919–1920, believed that in the presence of another vitamin (now known as vitamin A), that rickets sometimes developed in infants receiving large amounts of milk which they believed contained large amounts of these fat-soluble vitamins.

Sherman and Pappenheimer (3) in 1921 in their experiments showed that rickets may be caused by a disturbance in the mineral constituents of the foods eaten. In their diets they used vitamin-deficient foods of all types. Their experiments were not as conclusive as they might have been due to the fact that the animals used had not been completely depleted of their vitamin reserve. It has been shown experimentally that the body is capable of storing vitamins for future use.

About this time we find that Shipley, Park, McCollum and Simmonds (4) reported that the phosphate ions may have something to do with the apparent deficiency of calcium in the bones of the animals. In 1921–1922 these same investigators made a comparison of the relative protective value of butter fat and cod liver oil when given to albino rats on a low calcium diet. They reported that cod liver oil contains an abundance of some substance which directs the bone development and that it enables the animals to develop bones on a low calcium diet, but that butter contains only slight amounts of the substance.

From this time up to the present we find that the literature on vitamin D has grown so that it is possible to find as many as one thousand references on the subject in all of its various phases. Among some of the workers in the field we find the following: Windhaus, Steenbock, Hess, Hoppert, Humphrey, Bogert, Trail, Nelson, Huldschinsky, Hyole, Poulsson, Bills, Holmes and Bliss.

It is a generally accepted fact that this fat-soluble vitamin, vitamin D, is necessary in the diet in order to insure proper calcium metabolism. If absent in the diet of infants and very young children it causes malformation of the skeletal structure

* Scientific Section, A. PH. A., Madison meeting, 1933.

of the body and the disease is known as rickets. In the adult its absence is said to cause the condition known as osteomalacia.

During all of this experimental work it was found that sunshine was a good source of vitamin D, although certain conditions were necessary in order to get optimum results. Wyman (5) in 1927, working at the Children's Hospital in Boston, found that much of the ultraviolet light, which is the source or activator of the vitamin, would be lost unless certain filters were used, and he also noted that certain types of glass completely absorbed the ultraviolet light and prevented its passage into the room.

Steenbock (6) reported that the vitamin could be produced in foods that were exposed to the light from a mercury arc. This process is now known as the process of activation of foods. The process is protected by United States patents, and persons using the process are licensed by the Alumni Association of the University of Wisconsin who own the patent.

Since the sun is nature's source of vitamin D it can be stated that before man covered his body completely with clothing he no doubt obtained much of the vitamin from the sun. However, with the over-population of the large centers and with the advent of the custom of completely covering the body with clothing much of the beneficial effects of the sun rays were lost and more and more the human race became dependent upon the food supply for this vitamin.

We may well ask what has all this to do with the calcium distribution in the human body? If we consider the structure of the skin we will find that in the sub-epidermal layer of the skin there are layers of fat cells which contain cholesterol. This cholesterol becomes activated by the ultraviolet rays of the sun and in this way the body is furnished with the vitamin which in turn is absorbed by the skin capillaries and carried into the blood stream. This complex reaction then is thought to cause calcium deposition.

As has been stated modern man living primarily in the canyons of the large cities is for the most part deprived of nature's way of getting vitamin D. This causes the various conditions previously described and therefore the medical profession recognizing this fact has attempted to overcome these natural inequalities by adding to the diet substances rich in vitamin D, such as cod liver oil and other fish oils.

OBJECT OF THE INVESTIGATION.

The object of this investigation is to determine under what conditions can vitamin D be absorbed from the skin. This work was suggested by the work done by Hume, Lucas and Smith (7) in 1927. These investigators irradiated cholesterol and applied an oil solution to the test animals after first removing the hair of the animals and covering the spot so that the animals could not lap off any of the material. They found that some vitamin was absorbed from the skin. The author experienced some difficulty in using their technic on white rats, so during the course of the work a new method was developed which will be described in another place.

DEVELOPMENT OF EXPERIMENTAL RICKETS.

In order to produce experimental rickets the diet must be deficient in vitamin D, and it must also be abnormal in both calcium and phosphorus. It has been

found that when diets contain calcium and phosphorus in the ratio of 2 parts of calcium to 1 part of phosphorus that normal bone is formed, but when the ratio of calcium to phosphorus is very high, *i. e.*, 4 to 1 or higher, that they produce a type of rickets similar to that found in infants. Low calcium-high phosphorous diets will also produce rickets, but of a different type.

The standard ricket-producing diet of Steenbock, No. 2965, was used in the experiments. Its composition is as follows:

Diet No. 2965.

Yellow corn	76%
Wheat gluten	20%
Calcium carbonate	3%
Sodium chloride	1%

Calcium-phosphorus ratio: Ca:P = 4:1.

This diet is decidedly lacking in vitamin D and it has a high calcium to phosphorous ration, although by no means ideal in other respects it is sufficiently adequate to support growth and maintain satisfactory state of nutrition during the experimental period. The rats are placed on this diet from twenty-one to twenty-eight days or until they show definite symptoms of rickets as indicated by their gait, etc.

The animals are then lightly etherized and roentgengrams of the knee joints are taken. Care must be exercised not to give the animals an overdose of ether as it will kill them. This method of determining whether or not active rickets has developed in the animal checks each animal, thus assuring the rachitic condition of each animal, also the animal may be used for the repair diet. The latter and the former are advantages of this method over the line-test method. During the entire experimental period the animals are kept in darkened rooms, away from both daylight and sunlight.

THE REPAIR DIET.

Ordinarily the vitamin D containing material is either fed directly to the animals or it is mixed with the diet that is fed the animals. For the purpose of this work it is obvious that the material cannot be fed to the animals but must be applied to the skin and then absorbed through the skin if possible.

Among the materials used in this investigation are included the following: peanut oil, unirradiated cod liver oil concentrate in peanut oil containing 6000 A. D. M. A. units per Gm., cod liver oil, U. S. P., irradiated cholesterol in creams. The cream base consisted of vitamin D free substances as mineral oil, waxes and water. One cream contained 1000 A. D. M. A. units and the other 3000 A. D. M. A. units per 120 Gm., respectively.

AUTHOR'S RAT-TAIL METHOD.

Pieces of pyrex tubing of the proper diameter (this depends upon the size of the rat's tail) were cut in lengths so that when the rat's tail is inserted into the tube about seven-eighths of it is encased by the tube. The tube is sealed at one end and the other end is fire polished so that it will not cut the animal. The animal is

then weighed without the tube. The material is then spread on the rat's tail and the tail is then slipped into the tube. The tube is fastened to the animal by means of adhesive tape. The material is allowed to remain on the tail for twenty-four hours. Each day the animal is weighed and its weight noted, the tube being removed first and also any adhering material during the 10-day test period. The results obtained are of value only if the animal has consistently gained in weight during the repair diet period. All food fed the animals is weighed each day and the amount left by each animal is also noted.

Experiments were carried out on peanut oil in order to make sure that the peanut oil did not contain any vitamin D.

TABLE I.—RESULTS OF EXPERIMENT USING PEANUT OIL.

Series I, Rat No.	Weight of Rat Beginning Test.	Weight of Rat End of Test.	Gain in Weight.
462	50.7 Gm.	58.6 Gm.	7.9 Gm.
464	66.8 Gm.	72.4 Gm.	5.6 Gm.
465	58.5 Gm.	68.3 Gm.	9.8 Gm.
467	65.1 Gm.	74.0 Gm.	8.9 Gm.

From the above table it will be seen that these rats continued to gain in weight when peanut oil was added to their diet, although examination of the roentgengram photographs attached at the end of the tables shows that active rickets are still in progress and that the oil does not contain vitamin D.

RESULTS OF EXPERIMENT USING COD LIVER OIL CONCENTRATE DISSOLVED IN PEANUT OIL CONTAINING 6000 A. D. M. A. UNITS PER GRAM.

This material represents the unsaponifiable material from cod liver oil. Cod liver oil when treated with potassium hydroxide forms a soft soap. This soap when extracted with ether yields in the ether extract a fatty wax-like solid which is not soluble in water, but is soluble in alcohol, fats, oils and waxes. It is sterol in character and conforms to all of the requirements for a lipoid. It has a distinct fishy odor. The odor is fairly well disguised when dissolved in a bland oil-like peanut oil, although corn oil tends to accentuate the odor of the concentrate.

TABLE II.—COD LIVER OIL CONCENTRATE IN PEANUT OIL.

Series II, Rat No.	Weight of Rat Beginning of Test.	Weight of Rat End of Test.	Gain in Weight.
455	62.7 Gm.	66.6 Gm.	3.6 Gm.
457	58.1 Gm.	63.7 Gm.	5.6 Gm.
458	74.9 Gm.	81.5 Gm.	6.6 Gm.
459	55.9 Gm.	59.6 Gm.	3.7 Gm.
460	62.7 Gm.	70.1 Gm.	7.4 Gm.
461	57.3 Gm.	58.8 Gm.	1.5 Gm.

In this series excellent repair was noted as indicated by the photographs of the roentgengrams. The experiments show definitely that vitamin D can be absorbed from oil solution.

A comparison of the photographs of the roentgengrams taken of the hind legs of the animals used in Table III shows conclusively that cod liver oil, *i. e.*, the vitamin D from cod liver oil is absorbed from the skin.

TABLE III.—RESULTS OF EXPERIMENT USING COD LIVER OIL.

Series III, Rat No.	Weight of Rat Beginning of Test.	Weight of Rat End of Test.	Gain in Weight.
479	60.6 Gm.	69.9 Gm.	9.3 Gm.
480	50.3 Gm.	52.4 Gm.	2.4 Gm.
481	61.9 Gm.	66.8 Gm.	4.9 Gm.
482	62.4 Gm.	66.1 Gm.	3.7 Gm.
483	49.2 Gm.	53.5 Gm.	4.3 Gm.

The experiments to this point indicate that vitamin D can be absorbed from the skin. All of these tests, however, were performed on material of vegetable and animal origin. The author was interested in the effect of mineral oil on the absorption properties of the skin, and so several experiments were conducted on creams prepared from mineral oil, wax, water and borax. The results are indicated in the roentgengram photographs included in the report.

The technic followed is the same as that already described.

TABLE IV.—RESULTS OF EXPERIMENT USING MINERAL OIL BASE CREAM. CREAM CONTAINED 1000 A. D. M. A. UNITS PER 120 GM.

Series IV, Rat No.	Weight of Rat Beginning of Test.	Weight of Rat End of Test.	Gain in Weight.
472	62.8 Gm.	72.2 Gm.	9.4 Gm.
473	61.3 Gm.	64.9 Gm.	3.6 Gm.

TABLE V.—RESULTS OF EXPERIMENT USING MINERAL OIL BASE CREAM. CREAM CONTAINED 3000 A. D. M. A. UNITS PER 120 GM.

Series V, Rat No.	Weight of Rat Beginning of Test.	Weight of Rat End of Test.	Gain in Weight.
474	62.4 Gm.	72.0 Gm.	9.6 Gm.
475	58.1 Gm.	65.1 Gm.	7.0 Gm.

The experiments made on the absorption of vitamin D from the skin by Hume, Lucas and Smith (7) were performed on cholesterol that had been artificially irradiated. For sometime the author has been interested in the problem of sun irradiation. In his experiments he has found that several factors affect the success of the work. However, experiments have shown that the sun may be used as a source of vitamin D when the proper technic and apparatus is used.

The author has irradiated cholesterol and has incorporated this cholesterol in the cream base described above. The roentgengram photographs show that vitamin D may be obtained by the sun irradiation of cholesterol provided the cholesterol has not been highly purified. It was found that cosmetic creams containing irradiated cholesterol caused repair to take place in rachitic rats.

TABLE VI.—RESULTS OF EXPERIMENT USING SUN IRRADIATED CHOLESTEROL IN COSMETIC CREAM.

Series VI, Rat No.	Weight of Rat Beginning of Test.	Weight of Rat End of Test.	Gain in Weight.
476	55.1 Gm.	62.4 Gm.	7.3 Gm.
477	56.6 Gm.	61.1 Gm.	4.5 Gm.
478	60.0 Gm.	71.9 Gm.	11.9 Gm.

PHOTOGRAPHS OF ROENTGENGRAMS.

This part of the paper deals with the photographs of the roentgengrams taken of the knee prints of the experimental animals. The photographs that appear on

the left of the page under the title, "Beginning of the Test," indicate the stage of rickets developed in the animals due to being fed a diet deficient in vitamin D. In each case it will be noted that marked rickets are present.

The photographs that appear on the right of the page under the title, "End of the Test Period," represent the condition of the bones after the animal had been on a diet containing antirachitic material. With the exception of the experiments with peanut oil it will be noted that in each case the X-ray pictures show that distinct repair had been going on and in some instances complete healing had taken place.

At the request of the publication committee the author has only submitted one roentgengram photograph of a rat in each series. Other photographs will be sent to anyone interested in same.

The author feels that it is entirely possible to use this method in quantitating the amount of vitamin D in material containing the vitamin and he is at present conducting said experiments.

Photographs of roentgengrams indicating that peanut oil does not contain any antirachitic substances since no repair has taken place in the rachitic bones after the oil was added to the diet.

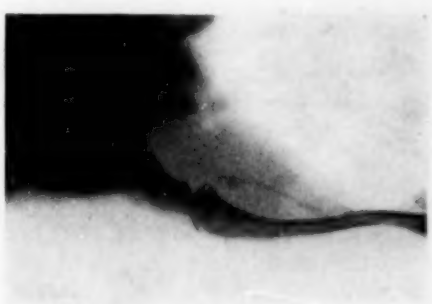
Beginning of Test. Series I, 465.

End of Test Period. Series I, 465.

Photographs of roentgengrams obtained in the experiments using cod liver oil concentrate in peanut oil, 6000 A. D. M. A. units per Gm.

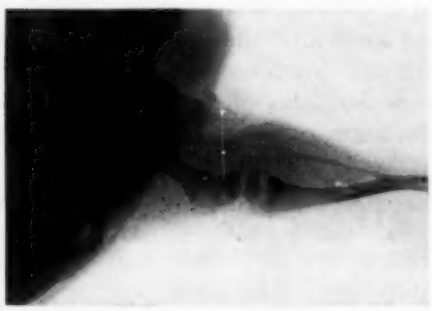
Beginning of Test. Series II, 458.

End of Test Period. Series II, 458.



Photographs of roentgengrams obtained in the experiments using cod liver oil, U. S. P. X.

Beginning of Test. Series III, 481.



End of Test Period. Series III, 481.

Photographs of roentgengrams obtained using a mineral oil base cream containing 1000 A. D. M. A. units per 120 Gm.

Beginning of Test. Series IV, 472.

End of Test Period. Series IV, 472.

Photographs of roentgengrams obtained using mineral oil base cream containing 3000 A. D. M. A. units per 120 Gm.

Beginning of Test. Series V, 474.

End of Test Period. Series V, 474.

Photographs of roentgengrams obtained using sun irradiated cholesterol in mineral oil cream base.

Beginning of Test. Series VI, 476.

End of Test Period. Series VI, 476.

PHOTOMICROGRAPHS.

In order to establish the extent of repair and also to approximate the extent of decalcification that had taken place in the experimental animal's bones the author felt that photomicrographs of the bone sections were necessary.

One of the hind legs of each animal was used for the purpose. After fixing in 10% formalin for 48 hours the legs were prepared for the "Celloidin Embedding" blocking process and sections of the bone were used to prepare microscopic mounts. Before mounting the sections in the usual routine manner, they were stained using "hematoxylin and eosin." Each photomicrograph represents about a 400 × magnification of the section.

Examination of the photomicrographs clearly shows the following: (1) the extent of decalcification that occurred in the bone during the development of experimental rickets, (2) the amount of repair or healing that took place during the ten-day repair period.

These photomicrographs also serve as a check on the roentgengram findings or interpretations. At the request of the editor of the JOURNAL and also the Committee on Publications these photomicrographs were omitted. However, anyone interested may receive them by writing to the author.

CONCLUSIONS.

1. The object of the thesis has been achieved, namely, that vitamin D can be absorbed from the skin. Also, the vehicle apparently has little or no effect in the absorption test, since the vitamin was absorbed from both vegetable and mineral oil bases.

2. In this investigation the author has developed a new method for the administration of vitamin D-containing substances, namely, the rat-tail method for the absorption of vitamin D.

3. That cosmetic creams may be used as a vehicle for carrying the vitamin substance has been demonstrated in two instances.

4. That the sun irradiation of cholesterol that has not been too highly purified is practical and that this material may be used as one of the sources of the vitamin.

5. Experiments are now under way for the quantitative estimation of vitamin D using the rat-tail method. This method may be of value in assay work.

6. It has been found that the presence of a small amount of vitamin A tends to produce more satisfactory results.

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MASSACHUSETTS COLLEGE OF PHARMACY.

FOOD AND DRUG LEGISLATION.

No very definite progress has been made in legislation before Congress on the various Food and Drug bills. The new Copeland bill, S. 2800, was voted a favorable report by the Senate Committee on Commerce after amending it in many particulars. The bill was reported to the Senate and has been printed in the Congressional Record for March 15th.

The bill contains a new provision for the discretionary appointment of advisory committees representing the several trades and the public, but no provision has been made for an administrative board of review, as strongly requested by the activities affected.

Other measures have not progressed and Senator Copeland is absent from Washington until about the end of March.

ASSAY FOR VITAMIN B COMPLEX IN THE PRESENCE OF INTERFERING SUBSTANCES.*

BY LLOYD K. RIGGS, B. J. G. CHIEGO, W. L. SAMPSON AND ANNABEL BEATY.

In the usual method of assay for the vitamin B complex young rats are starved for this complex until a sharp decline of weight is observed. The minimum dose of the material under investigation, necessary to restore a normal rate of growth, is then determined.

In applying this method the following factors may well be taken into account: (1) The accuracy of the method must obviously depend somewhat upon the nicety of judgment as to whether the normal rate of growth is restored or not. (2) The interpretation of results is facilitated by the use of a physical standard of reference, a material of well-known vitamin B complex potency, to which all assays for this vitamin complex may be referred. (3) The method is not quite generally applicable because of the fact that some food and medicinal products contain salts, drugs, laxatives, poisons or odd flavoring materials, which experimental animals either refuse to eat or from which complicated abnormal or ill effects follow. In other specimens, the vitamin is in such dilution that a concentration must be made.

1. TEST FOR THE RESTORATION OF NORMAL RATE OF GROWTH.

It is frequently observed that litter mates of the same sex do not grow at the same rate even when kept under identical conditions of housing and diet. When animals which have declined in weight due to starvation for the vitamin B complex are fed on several different doses of a given test material, animals on different doses may all gain in weight but it is frequently difficult to be certain that any one animal has been restored to its individual normal growth rate. This element of uncertainty may be eliminated if at the end of the test period all test doses are discontinued and each animal is then given a daily dose of dried brewers' yeast which is known to be several times the minimum amount required for normal growth. The growth curves of the animals are then followed for a week or two. If the curve breaks upward with the feeding of the brewers' yeast, the previous dose of the test material was inadequate. If the growth curve continues as when the previous dose was given, the previous dose was adequate for normal growth.

2. PHYSICAL STANDARDS OF REFERENCE.

In order to overcome the known variation in the response of animals to vitamin feeding this laboratory has adopted the procedure of making assays for the vitamin B complex comparative. Various doses of a material to be tested for the vitamin B complex are fed in comparison with fresh bakers' yeast cake (Fleischmann) and dried brewers' yeast (Harris). Only a few animals need to be placed on doses of the yeast cake or of dried brewers' yeast, because it has been learned from several years of experience that 1500 mg. of the fresh yeast cake is approximately equivalent to 100 mg. of the dried brewers' yeast and that the vitamin B complex potency of these doses is just about adequate for normal growth of young rats. It is also the experience of this laboratory that the dried brewers' yeast, when kept in closed con-

* Scientific Section, A. PH. A., Madison meeting, 1933.

tainers, shows no detectable variations in potency over a period of about three years. This material has, therefore, been adopted as a standard of reference for this laboratory. The general adoption of some such standard would greatly facilitate interpretation of the results obtained by different laboratories.

3. ASSAY OF A FOOD MATERIAL WHICH ANIMALS DO NOT EAT READILY.

An attempt was made to assay the vitamin B complex in bouillon cubes[1] prepared from an extract of brewers' yeast and presumably containing vitamin B. On account of the salts and flavoring of these cubes, experimental animals refused, after the first few days of the test, to eat the portions of bouillon cube supplied to them, either in the form of small (weighed) pieces of the cube or as similar amounts of the cube material mixed with some inert substance such as starch or dextrin. For purposes of assay it was therefore necessary to devise some method for the extraction of the vitamin-bearing constituents of the bouillon cubes.

The approximate composition of the bouillon cubes is indicated in the following table (Table I).

TABLE I.

Moisture	5.84%
Nitrogen	3.54
Protein ($N \times 6.25$)	22.13
Ash	61.35
NaCl	55.02

I. EXTRACTION EXPERIMENTS OF BOUILLON CUBES.

A survey of the literature dealing with the properties of the vitamin B complex lead to a consideration of the three following possible methods for the extraction of the vitamin B bearing material from bouillon cubes.

1. Extraction with dilute alcohol (approximately 70%).
2. Adsorption of the vitamin on fuller's earth
3. Extraction of the vitamin-bearing material with glacial acetic acid.

Method No. 1 was tried and discarded because it was found that a complete extraction by this method required repeated extractions and chilling of the extract in the refrigerator over night. Such procedure results in so much exposure of the extract to the influence of atmospheric oxygen as to very largely destroy the vitamin B present in the original cube material.

Method No. 2 was tried and discarded because it was found that while it was very easy to adsorb a portion of the vitamin-bearing material on fuller's earth, there appeared to be no satisfactory way in which we might be assured that the vitamin-bearing material was quantitatively adsorbed. The probability of a selective adsorption of the vitamin B factors was also taken into consideration.

Method No. 3—extraction with acetic acid—was finally adopted for use in this series of studies. The method, as first tried, gave rather irregular results because of apparent differences in the amount of exposure to the air which occurred in the preparation of different batches of the extract. A standardized procedure finally

[1] Yeast Bouillon Cubes—Harris, prepared by the Harris Laboratories, Tuckahoe, New York.

was selected, after repeated trials, which yields rather uniform results. This method of extraction is briefly described below.

Ten bouillon cubes, weighing on the average 45 Gm., are crushed in a small mortar and washed into a small beaker with 135 cc. of glacial acetic acid. The cubes and acid are heated as rapidly as possible, with constant stirring, to boiling. As soon as the mixture is boiling vigorously, the beaker is removed from the burner and the acetic acid-insoluble material is allowed to settle for a few moments. The clear, supernatant liquor is then decanted through a funnel in which a filter mass of absorbent cotton has been previously moistened with glacial acetic acid.

As soon as a small amount of the filtrate (acetic acid extract) is obtained, it is drawn, little by little, by vacuum, into a 150-cc. weighed distillation flask. The acetic acid extract is drawn into the distilling flask through a glass tube drawn out to a capillary so that the acetic acid solution falls into the flask a few drops at a time and evaporates almost as rapidly as it is delivered to the flask. The flask is immersed in a water-bath kept at a temperature of 70° C. The flask is connected by means of a Liebig condenser with a vacuum pump so that the acetic acid is distilled off under a high vacuum.

The residue remaining in the beaker after the first extraction is again extracted with 100 cc. glacial acetic acid and the acetic acid solution is decanted through the same filter into the same receiving flask. The residue from this extraction is again similarly extracted twice with 50-cc. portions of glacial acetic acid and then once extracted with 25 cc. of glacial acetic acid. The final portion of acetic acid (25 cc.) is practically colorless and serves the purpose of removing all but the last traces of the acetic acid-soluble material which remains on the cotton filter through which each extract is poured.

The vacuum distillation is continued during the time that the several extractions are being made, so that at the time the final extraction is completed, only a small amount of the acetic acid solution remains to be distilled. As soon as all of the acetic acid solution has been transferred to the distilling flask, the inlet tube is connected to a reservoir of nitrogen gas and the distillation is continued under a stream of nitrogen until the final volume of the material in the flask has been reduced to approximately 60 cc.

At this point in the procedure the flask is removed from the hot water-bath and the flask is cooled with either tap water or ice water. The flow of nitrogen gas is continued during the cooling of the flask. When the flask is cool, starch is added to the semi-solid residue and the flask is placed in a vacuum desiccator over sodium hydroxide sticks. The desiccator is evacuated under the highest possible vacuum and the mixture of starch and extract of the cubes is allowed to remain in the flask in the desiccator for two days. At the end of two days' time the vacuum is released with dry nitrogen gas and the flask with its contents is removed and accurately weighed. The weight of the flask alone was taken before the experiment was begun. Additional starch is now added in an amount which will bring the contents of the flask to three times the weight of the ten cubes taken for the extraction.

It is obvious that three Gm. of the mixture of starch and cube extract now contains approximately the same amount of acetic acid-soluble material as was contained in one Gm. of the original cube. This is the material that is fed to the experimental animals in testing the vitamin B (complex) potency of the bouillon

cubes. If, then, we assume that all of the vitamin B complex is soluble in acetic acid and if we further assume that no losses have occurred during the laboratory manipulations to which the material has been subjected, we may then assume that the vitamin B complex potency of the starch mixture represents the vitamin B complex potency of the original bouillon cube in the proportion of three to one. There is apparently no simple way in which the validity of the two essential assumptions upon which the third assumption is based, may be definitely verified. It is almost certain that the second assumption is not entirely correct, because we find that if any delay in the extraction and distillation procedure occurs, a less potent vitamin extract is obtained. A more correct statement of this assumption might then well be that, by standardizing as nearly as possible our procedure and making our extractions as rapidly as possible and with as little exposure to air as possible, we are able to make the extraction with a minimum loss of vitamin B complex potency.

TABLE II.—GROWTH OF ANIMALS ON TEST DOSES—EFFECT OF SURPLUS OF BREWERS' YEAST.

Animal.	Material Fed.	Daily Dose in Mg.	Days on Given Dose.	Total Weight Change.	Daily Weight Change.	Dose of B. Y. in Mg.	Days on B. Y.	Total Weight Change.	Daily Weight Change.
7 F	B. Y.	25	54	27	0.5	1000	26	37	1.423
8 M	B. Y.	50	54	56	1.037	1000	26	54	2.076
2 F	B. Y.	50	53	44	0.8301	1000	26	35	1.346
1 M	B. Y.	100	53	90	1.698	1000	26	36	1.384
19 M	B. Y.	100	53	95	1.792	1000	26	41	1.576
4 F	B. Y.	150	55	62	1.127	1000	13	11	0.8461
23 M	B. Y.	150	52	81	1.553	1000	27	48	1.777
6 M	B. Y.	200	50	90	1.800	1000	12	11	0.9166
17 M	B. Y.	200	50	90	1.800	1000	12	22	1.833
27 M	Y. B. C.	100	54	11	0.2037	1000	26	87	3.346
10 F	Y. B. C.	100	54	− 3	−0.055	1000	26	56	2.153
12 F	Y. B. C.	100	54	11	0.2037	1000	26	53	1.203
15 F	Y. B. C.	200	54	33	0.6111	1000	26	56	2.153
13 M	Y. B. C.	200	54	31	0.5740	1000	26	77	2.961
29 M	Y. B. C.	300	56	60	1.071	1000	26	50	1.923
22 F	Y. B. C.	300	54	68	1.259	1000	26	21	0.8076
28 F	Y. B. C.	400	56	56	1.000	1000	26	23	0.8846
3 F	Y. B. C.	400	56	55	0.9821	1000	26	19	0.7307
20 F	F. Y. C.	500	54	23	0.4259	1000	27	45	1.666
9 M	F. Y. C.	500	34	12	0.3527	Died at end of 34 days			
30 M	F. Y. C.	1000	54	55	1.018	1000	27	74	2.740
11 M	F. Y. C.	1000	54	28	0.5185	1000	27	28	1.036
21 M	F. Y. C.	1000	54	58	1.036	1000	27	60	2.222
24 M	F. Y. C.	1500	54	61	1.129	1000	27	31	1.148
26 F	F. Y. C.	2000	50	43	0.8600	1000	26	14	0.5384
25 F	F. Y. C.	2000	54	56	1.036	1000	27	24	0.8888

NOTE: B. Y. = Brewers' Yeast, Y. B. C. = Yeast Bouillon Cube, F. Y. C. = Fleischmann's Yeast Cake.

From the above it appears to us that the minimum vitamin B complex dose for normal growth of the young, white rat is as follows:

Brewers' yeast	100 mg.
Bouillon cubes	300 mg.
Yeast cake	1500 mg.

II. ANIMAL EXPERIMENTS.

Some seventy-five animals were used in establishing the relative vitamin B complex potency of dried brewers' yeast (Harris), fresh yeast cake (Fleischmann) and yeast bouillon cube (Harris). It is not necessary to present the complete data obtained from all of these animals because the complete data are in strict conformity with the data of one typical test, using twenty-six animals, and employing the technic described above. The data of this test are presented in Table II.

It will be noted from the data of Table II that those animals that received daily doses of less than 100 mg. of brewers' yeast; less than 300 mg. of yeast bouillon cube and less than 1500 mg. of fresh yeast cake, when changed from the test doses to 1000 mg. of brewers' yeast showed a daily gain of weight greater than the daily gain of weight on the test doses. Those animals receiving daily doses of at least 100 mg. of brewers' yeast; 300 mg. of yeast bouillon cube and 1500 mg. of yeast cake do not show a marked increased rate of gain when transferred to 1000 mg. of brewers' yeast.

From these observations it is possible to draw the conclusions that 100 mg. of the dry brewers' yeast, 300 mg. of the material of the yeast bouillon cubes, and 1500 mg. of the fresh yeast cakes are each adequate for the normal growth of rats for the period of this test.

The vitamin B complex potency of yeast cakes and the yeast bouillon cubes used in these studies may be expressed in terms of the potency of the physical standard[1] employed in this laboratory as follows:

$$\frac{\text{Minimum adequate dose of the standard}}{\text{Minimum adequate dose of bouillon cube}} = \frac{100}{300} = \frac{1}{3}$$

The bouillon cube then has a vitamin B complex potency of 33% that of the standard.

$$\frac{\text{Minimum adequate dose of the standard}}{\text{Minimum adequate dose of yeast cake}} = \frac{100}{1500} = \frac{1}{15}$$

The yeast cake then has a vitamin B complex potency of 6.6% that of the standard.

If one wishes to reduce the figures obtained to the basis of the dry materials contained in each product, it is only necessary to take into account the fact that the brewers' yeast contains approximately 1% moisture and that the bouillon cubes and the yeast cakes contain approximately 5.8% and 66% moisture, respectively. Thus 99 mg., 286 mg. and 495 mg. of the dry material of brewers' yeast, of bouillon cube and of yeast cake, respectively, may each be said to contain one adequate dose of the vitamin B complex which might well be called one unit of the vitamin B complex.

It might be well to point out that one bouillon cube weighs approximately 4.5 Gm. (4500 mg.) and that one yeast cake weighs approximately 12.5 Gm. (12,500 mg.). One bouillon cube will then contain:

$$\frac{4500}{300} = 15 \text{ units of the vitamin B complex}$$

[1]Dried brewers' yeast—Harris.

One yeast cake will then contain:

$$\frac{12{,}500}{1500} = 8.33 \text{ units of the vitamin B complex.}$$

We have found that a simple and convenient method for the graphic representation of the growth of animals which have been used in a test employing the technic described above is to lay off on cross section paper a line representing the weight during the test period, *i. e.*, a line joining the graphic points representing the weights at the beginning and the end of the test period. A second line representing the weight of the animal during the period in which the excessive dose of brewers' yeast is fed is similarly laid off on the same paper. The angle at which

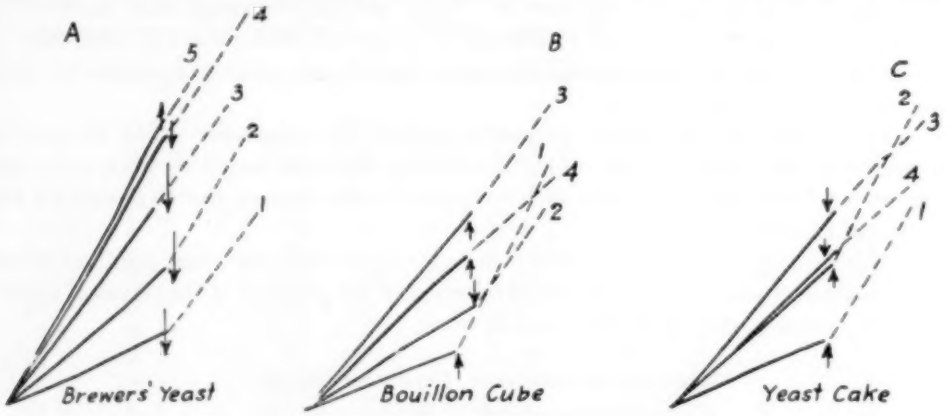

Fig. 1.

Curves No. 1, 2, 3, 4 and 5, division A, of Fig. 1 are constructed from the composite weight figures of animals fed on 25, 50, 100, 150 and 200 mg. of brewers' yeast, respectively. Arrows indicate the feeding of 1000 mg. of brewers' yeast. Curves 1, 2, 3 and 4, division B, represent animals on 100, 200, 300 and 400 mg. of bouillion cube. Curves 1, 2, 3 and 4, division C, represent animals fed on 500, 1000, 1500 and 2000 mg. of fresh yeast cake. The upward breaks in curves 1 and 2 of each series indicate:

25 mg. brewers' yeast is inadequate for normal growth.
50 mg. brewers' yeast is inadequate for normal growth.
100 mg. bouillon cubes is inadequate for normal growth.
200 mg. bouillon cubes is inadequate for normal growth.
500 mg. yeast cake is inadequate for normal growth.
1000 mg. yeast cake is inadequate for normal growth.

these lines intersect indicates any change in the rate of growth during the two periods. In cases in which several animals are on each dose, the composite weight figures for the several animals may conveniently be used in the construction of such figures.

The composite weight figures for the animals employed in this test were used for the construction of Fig. 1.

SUMMARY.

1. A simple method is described for the extraction of the vitamin B complex bearing material from such food products as bouillon cubes prepared from an extract of yeast. This extraction is by means of glacial acetic acid. The acetic acid is removed by distillation in vacuum and in a stream of inert gas such as nitrogen.

The paste remaining in the distillation flask is mixed with starch and aliquot parts of the starch mixture are fed as known doses of the material of the bouillon cube.

It is obvious that this method will be inapplicable for the separation of the vitamin B complex from interfering substances which are soluble in glacial acetic acid.

2. A simple method is described which employs each test animal used in an assay for the vitamin B complex as its own control. Experimental animals, depleted of the vitamin B complex, are fed on given doses of the material to be tested. At the end of the test period a daily dose of a material (dried brewers' yeast) known to contain several times the minimum adequate dose of the vitamin B complex required for normal growth is substituted for the daily dose of the test material under investigation. If the growth curve breaks upward with the feeding of the large dose of brewers' yeast, the given dose of the test material was inadequate for normal growth.

3. Dried brewers' yeast known to be stable for a period of at least three years is suggested as a physical standard of reference of assays for the vitamin B complex.

4. It has been found that 100 mg. of brewers' yeast, 300 mg. of bouillon cube and 1500 mg. of yeast cake are equivalent in vitamin B complex potency.

LABORATORIES OF THE RUTGERS UNIVERSITY,
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THE COLORIMETRIC AND ELECTROMETRIC p_H DETERMINATIONS OF SOLUTIONS OF CERTAIN ALKALOIDAL SALTS.*[1]

BY ALLEN F. PETERS, B.SC., AND ARTHUR OSOL, PH.D.

A review of the literature reveals several reports of investigations on the determination of the hydrogen-ion concentration of solutions of alkaloidal salts. Evers (1) determined the colorimetric p_H values of solutions of the pure hydrochlorides of morphine, quinine and atropine and suggested the use of certain indicators which would give more accurate results in the titration of the corresponding free alkaloids. McGill (2), and later Wagener and McGill (3), using electrometric methods of measurement, obtained values for pure quinine, morphine, strychnine and atropine salts. Krantz (4), using a hydrogen electrode, determined the p_H values of pure quinine hydrochloride and also obtained data on the p_H values of quinine, strychnine and atropine dissolved in varying quantities of tenth-normal hydrochloric acid in excess.

Masucci and Moffat (5) reported electrometric values for many commercial samples of morphine, codeine, quinine, strychnine, atropine and caffeine salts. Wales (6) determined titration curves for various alkaloids and from these he obtained p_H values for pure salts. Based on the latter, he recommended the use of certain indicators to minimize titration errors. Finding great variations in commercial samples of alkaloidal salts, Eder (7) recommended the adoption of definite p_H limits for alkaloidal salt solutions. More recently, Mellon and Tigelaar (8)

* Abstracted from the thesis of Allen F. Peters, submitted to the Faculty of the Philadelphia College of Pharmacy and Science in partial fulfilment of the requirements for the degree of Master of Science in Chemistry. [1] Scientific Section, A. PH. A., Madison meeting, 1933.

compared the results of alkaloidal titrations using various indicators and constructed titration curves for atropine, strychnine and brucine.

As many of the measurements reported in previous investigations were obtained from titration curves the authors of this paper considered it advisable to prepare certain pure salts from the corresponding pure alkaloids and to determine electrometric and colorimetric values of solutions of the salts. The effect of dilution was likewise considered to be worth while investigating. The results obtained in a study of this kind would be of value in setting p_H standards for testing for the presence of excess acidity or alkalinity in alkaloidal salts.

EXPERIMENTAL.

Pure brucine sulphate, strychnine hydrochloride, strychnine sulphate, quinidine sulphate and quinine sulphate were prepared by shaking a nearly saturated chloroform solution of the pure alkaloid with a quantity of the proper acid equivalent to approximately 75% of the alkaloid used. The concentration of acid was sufficiently high to produce precipitation of the alkaloidal salt in the aqueous solution. After filtration on a Büchner funnel, the salt was successively washed with chloroform, alcohol and water. The residue was recrystallized from hot water, filtered, washed with water and dried between filter papers.

Quinine bisulphate, quinine hydrochloride, quinine and urea hydrochloride and quinine hydrobromide were purified by repeated crystallization of commercial samples.

The indicators listed in the tables were those which could be most easily matched with the standards. Although slight precipitation was observed with certain solutions in the higher concentration range, the matching of colors was easily made.

The results given for the electrometric determinations were calculated from electromotive force measurements of quinhydrone and tenth-normal calomel electrode combinations. In the case of the higher concentrations of alkaloidal salt, the electromotive force measurements did not attain equilibrium, hence no p_H values are given in the tables. While the cause of the instability of the potential is not known, it is, perhaps, connected with the precipitation which occurs in all solutions upon the addition of quinhydrone. In the most dilute solutions the precipitation can be seen only with difficulty and the electromotive force remains constant within one or two millivolts, but with increasing salt concentration the precipitation becomes very noticeable and the potential too unsteady to measure. Measurements made with hydrogen electrodes were, in general, also unsatisfactory.

TABLE I.—p_H OF QUINIDINE SULPHATE SOLUTIONS.

Per Cent Salt.	Colorimetric p_H (Chlorphenol Red).	Electrometric p_H.	Commercial Sample.
0.25	6.4	6.33	6.2
0.50	6.4	6.35	6.3
1.00	6.5	6.39	6.4

These values for quinidine sulphate are in good agreement with a value of 6.1 obtained by Wales (6) from titration curves for this salt.

In Table I and the following tables are set forth the results of the p_H determinations of pure salts as well as commercial samples. The water used in preparing the solutions was freshly distilled and was found to have a p_H of 6.2 when tested with isohydric chlorphenol red. Solutions made with distilled water of $p_H = 5.7$ as well as solutions through which carbon dioxide-free nitrogen was bubbled rarely differed by as much as 0.1 p_H unit from the values given in the tables.

TABLE II.—p_H OF QUININE SULPHATE SOLUTIONS.

Per Cent Salt.	Colorimetric p_H (Chlorphenol Red).	Electrometric p_H.	Commercial Sample.
0.025	6.2	6.26	5.7
0.050	6.2	6.22	5.6
0.100	6.2	6.21	5.6

The values given in Table II are practically identical with the results obtained by Wales for quinine salts of strong acids, namely, 6.12.

TABLE III.—p_H OF QUININE HYDROBROMIDE SOLUTIONS.

Per Cent Salt.	Colorimetric p_H (Chlorphenol Red).	Electrometric p_H.	Commercial Sample.
0.10	6.2	6.34	5.8
0.25	6.2	6.29	5.9
0.50	6.2	6.26	6.0
1.00	6.3	6.24	6.2
2.00	6.4	6.21	6.2

Here again the values are comparable with that given by Wales for quinine salts. It should be pointed out that the colorimetric values increase while the electrometric values decrease slightly with increasing salt concentration. The discrepancy, which is rather small, probably originates in the neglect of salt effects in both the electrometric and colorimetric methods, as well as the precipitation which occurs when quinhydrone is used.

TABLE IV.—p_H OF QUININE HYDROCHLORIDE SOLUTIONS.

Per Cent Salt.	Colorimetric p_H (Chlorphenol Red).	Electrometric p_H.	Commercial Sample.
0.10	6.1	6.33	6.3
0.25	6.2	6.30	6.3
0.50	6.2	6.21	6.4
1.00	6.2	6.17	6.5
2.00	6.3	6.10	6.5
3.00	6.4	....	6.5
5.00	6.4	....	6.5

The corresponding values obtained by Krantz were 6.19 and 6.15 for 0.1% and 0.8% solutions, respectively, while McGill reported values of approximately 6.0.

TABLE V.—p_H OF QUININE BISULPHATE SOLUTIONS.

Per Cent Salt.	Colorimetric p_H (LaMotte Yellow).	Electrometric p_H.	Commercial Sample.
0.10	3.6	3.54	3.6
0.25	3.6	3.38	3.6
0.50	3.6	3.30	3.6
1.00	3.6	....	3.5
2.00	3.5	....	3.5
5.00	3.5	....	3.4

No values for quinine bisulphate are available for comparison but Evers reports a value of 3.40 for quinine dihydrochloride.

TABLE VI.—p_H OF QUININE AND UREA HYDROCHLORIDE SOLUTIONS.

Per Cent Salt.	Colorimetric p_H (LaMotte Yellow).	Electrometric p_H.	Commercial Sample.
0.10	3.6	3.62	3.6
0.25	3.6	3.51	3.6
0.50	3.5	3.40	3.6
1.00	3.5	3.30	3.6
2.00	3.5	....	3.6
5.00	3.5	....	3.6

TABLE VII.—p_H OF BRUCINE SULPHATE SOLUTIONS.

Per Cent Salt.	Colorimetric p_H (Chlorphenol Red).	Electrometric p_H.	Commercial Sample.
0.10	5.6	5.74	7.5
0.25	5.5	5.70	7.6
0.50	5.4	5.63	7.7
1.00	5.3	5.52	...

For brucine salts Wales reports a value of 4.85.

TABLE VIII.—p_H OF STRYCHNINE HYDROCHLORIDE SOLUTIONS.

Per Cent Salt.	Colorimetric p_H (Chlorphenol Red) (Methyl Red).	Electrometric p_H.	Commercial Sample.
0.50	5.6	5.62	6.1
1.00	5.5	5.42	6.2
1.50	5.4	5.35	6.2
2.00	5.3	5.16	6.3
2.50	5.3	5.12	6.3

Again Wales' value for strychnine, 4.81, is lower than the values given in this table. However, McGill (2) reports values of 5.45 and 5.42 for 0.002 and 0.02 normal strychnine solutions, respectively.

TABLE IX.—p_H OF STRYCHNINE SULPHATE SOLUTIONS.

Per Cent Salt.	Colorimetric p_H (Chlorphenol Red).	Electrometric p_H.	Commercial Sample.
0.50	5.8	5.83	5.2
1.00	5.8	5.74	5.1
1.50	5.7	5.68	5.0
2.00	5.6	5.61	5.0

From an inspection of Table IX it is evident that a slight difference exists between the values for strychnine hydrochloride and strychnine sulphate. Whether or not the difference is real cannot be answered definitely.

CONCLUSIONS.

We have determined the electrometric and colorimetric p_H values of several pure alkaloidal salts. Because of the precipitation which occurs when quinhydrone is added to the solutions, it is recommended that the colorimetric method should be used for routine work in testing for acidity or alkalinity of the salts reported in this paper.

It has been found that, in general, the p_H values for a given salt solution are practically constant over a wide range of concentration.

For a given alkaloidal base, it has been found that variation of the anion produces little if any change in the p_H values of solutions of the salt, provided the anion is of the strong acid type.

It has been shown that the p_H values obtained from measurements of pure salt solutions are, in general, in good agreement with values obtained from titration curves.

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LABORATORY OF PHYSICAL CHEMISTRY,
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PHILADELPHIA, PA.

NOTICE: RESEARCH WORKERS IN PHARMACY.

The returns for the 1934 census of Research in Pharmacy intended for publication are now being taken. If any research worker has not received a blank, or if returns have not been made by workers to whom blanks have been sent, it is requested that they immediately write to JAMES C. MUNCH, 40 North Maple Avenue, Lansdowne, Pa., sending their name, business address and the names of the specific problems, with their nature, which are being studied. In order to facilitate completion of this report it is urged that this information be sent at once.

The American Institute of Pharmacy.

To be dedicated during the week of May 7th. The landscaping has not been completed, but is well under way. The lighting fixtures outside are of bronze as are the main doors, each weighing 1000 pounds. Carved urns, exquisitely done out of a block of solid white marble, flank the main entrance. The panels on either side of the main entrance are indicative of pharmacy and its service.

THE EFFECT OF ETHYLENE GLYCOL ON THE SERUM CALCIUM OF THE RABBIT.*

BY JAMES M. DILLE.

A report of work done under the direction of C. L. Wible College of Pharmacy, University of Nebraska, in partial fulfilment of the requirement for the degree of Master of Science in Pharmacology.

Ethylene glycol, commonly known as glycol, is a diatomic alcohol which stands midway between the monatomic alcohol, ethanol, and the triatomic alcohol, glycerol. Because of this relation it has been suggested as a substitute for these two compounds. It has been used as a preservative of fruit juices and extracts, and in non-intoxicating beverages (1). It has also been introduced as a vehicle for certain medicinal compounds not easily soluble in water. Its use as a vehicle for iodobismuthite is an example of this.

Ethylene glycol when used in the above ways has been considered harmless. Reid Hunt (2), (3), however, has seriously doubted this, while Hanzlik (4) claims toxicity only in large amounts which are never given for therapeutic purposes.

Hunt claims that the toxic effects of ethylene glycol are due to oxalic acid formed by the oxidative processes of the body. This seems to be true because the presence of oxalic acid can be demonstrated in the urine after the administration of ethylene glycol (5), (6). Calcium oxalate is present in the renal calculi formed by the administration of small amounts of ethylene glycol given over a long period of time.

In this work it has been assumed that if oxalic acid is formed it will precipitate the calcium of the blood as an insoluble salt, and thus cause a fall in the calcium content of the blood.

EXPERIMENTAL.

The experimental work was divided into two parts. In the first part the calcium changes occurring as the result of the administration of toxic doses were determined. The rabbit was starved 24 hours to eliminate the changes due to ingested food. At the end of this period the first blood sample was taken. The glycol was then administered and the samples of blood taken at approximately 15-minute intervals for the first hour, and then at half or hour intervals until death occurred.

In order to determine the effect of excessive loss of blood on the calcium level a control rabbit was run for each experiment. Physiological saline was administered instead of ethylene glycol. Samples of blood were taken at the same intervals as in the experimental animal.

Four experiments of this sort were run. In two of them the glycol was administered intraperitoneally, in the other two the intravenous method was used.

All four of these experiments checked each other closely. The results of a typical experiment are embodied in Table I and Fig. 1.

In the second part of the experimental work the effects of small doses of ethylene glycol given over a period of time were determined.

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* Scientific Section, A. PH. A., Madison meeting, 1933.

TABLE I.—ACUTE TOXICITY.

Control Rabbit A-7. Weight—2.84 Kg. Dose—4.5 cc. of sterile saline per Kg. by intravenous injection.			Experimental Rabbit A-8. Weight—2.32 Kg. Dose—4.5 cc. of ethylene glycol per Kg. by intravenous injection.		
Time.	Calcium.	Hmgb.	Remarks.	Calcium.	Hmgb.	Remarks.
9:00	14.4 mg.	80		13.1 mg.	85	
9:10	Inject saline			Inject ethylene glycol		
9:30	13.7 mg.	80		12.8 mg.	85	Accel., resp.
9:45	13.8 mg.	80		12.5 mg.	80	.. ..
10:00	13.8 mg.	80		12.6 mg.	80	.. ..
10:30	14.2 mg.	80	No distinctive	13.2 mg.	80	Resp. norm.
11:00	14.1 mg.	75	changes from	12.8 mg.	80	
11:30	14.0 mg.	75	normal.	12.7 mg.	75	
12:00	14.2 mg.	70		13.2 mg.	70	Slight depr.
1:00	14.0 mg.	70		13.0 mg.	70	.. ..
3:00	14.5 mg.	60		13.2 mg.	60	.. ..
6:00	13.8 mg.	60		13.0 mg.	50	Depression
8:00	13.2 mg.	50		12.0 mg.	45	Coma
8:35				Dead		

No abnormal conditions observed in a gross examination of various organs.

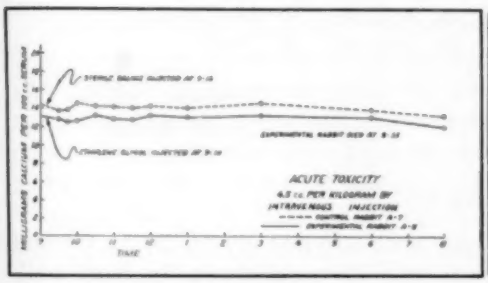

Fig. 1.

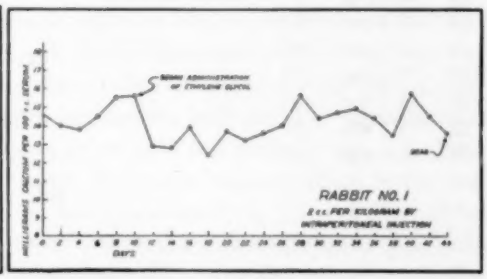

Fig. 2.

Calcium determinations were made on nine rabbits over a period of two weeks. These were made every other day. The daily administration of ethylene glycol was begun at the end of this two-week control period. The intraperitoneal method of injections was used. The rabbits were given doses varying from 3 to 4 cc. of glycol per Kg. per day.

Diet is the cause of much variation in serum calcium, and in order to keep this as constant as possible, a diet of cabbage and oats was fed. An excess of food was kept in the cage at all times. The animals were kept on this diet a few days before starting the experimental period.

A great deal of variations was encountered both in the control period and in the period during which the glycol was administered. The accompanying table (Table II) and graph (Fig. 2) may be considered typical of the results obtained in this part of the experimental work.

In order to determine whether or not any deleterious results might occur from the loss of blood, hemoglobin determinations were made at the same time that the blood was collected. In rabbits receiving the acute dose, the fall in the experimental animal was paralleled by a fall in the control rabbit. In experiments on

chronic intoxication the hemoglobin remained constant during the two weeks' control period. This indicates that the loss of blood required for the calcium determinations had no serious effect on the serum calcium. After the administration of the glycol the hemoglobin fell.

Serum calcium was determined by the method of Kramer and Tisdall (7), (8), using the modified washing technique of Clark and Collip (9). This is a volumetric procedure. Calcium is precipitated from the serum, after the removal of the proteins, as calcium oxalate. The precipitate is dissolved in sulphuric acid and titrated at 70° C. against 0.01*N* potassium permanganate.

TABLE II.

RABBIT NO. 1.

Chronic Intoxication.

Days.	Calcium.	Hmgb.	Remarks.
0	14.6 mg.	..	
2	14.0 mg.	..	
4	13.8 mg.	..	
6	14.5 mg.	75	
8	15.5 mg.	80	
10	15.6 mg.	80	Begin admin. 2 cc. per
12	12.9 mg.	70	Kg. daily
14	12.8 mg.	70	
16	13.9 mg.	60	
18	12.4 mg.	55	
20	13.7 mg.	50	
22	13.2 mg.	50	
24	14.6 mg.	50	
26	14.0 mg.	50	Some depression
28	15.6 mg.	50	
30	14.4 mg.	50	Depression
32	14.7 mg.	45	
34	14.9 mg.	50	
36	14.4 mg.	45	
38	13.5 mg.	40	Weak
40	15.7 mg.	45	Weak
42	14.5 mg.	40	Very weak
44	13.6 mg.	40	Dead
			Postmortem showed no adhesions, viscera appeared normal. Stomach filled.

DISCUSSION.

Our experimental work seems to indicate that ethylene glycol has no marked effect on serum calcium. This is established with fair certainty in the work with toxic doses. Such variations as were present in the experimental animal were paralleled by variations over a similar range in the control.

In the work involving the continuous administration of small doses, extensive fluctuations were noted throughout the course of the experiment, both in the control and experimental period. These variations are probably due to diet. It was thought that this could be minimized by keeping the diet as constant as possible, but this proved difficult. McBorne and Campbell (10) state that normally the fluctuations of serum calcium may amount to as much as 5 or 6 mg. per 100 cubic centimeters of serum. Our variations over the entire period of the experiment amounted to 4 or 5 mg.

Naturally it follows that any change in calcium due to the effect of ethylene glycol must needs be greater than the range of normal variations in order to be detected. Therefore if there is any change, it is so small as to be covered by the normal variations.

Oxalic acid is undoubtedly formed because in no other way can the presence of oxaluria, and calcium oxalate in the renal calculi be easily explained. From our work we believe that the ethylene glycol is oxidized to oxalic acid so slowly that any change in serum calcium is too small to be easily detected.

CONCLUSION.

Variations in serum calcium of the rabbit do not depart from normal with the administration of ethylene glycol in toxic amounts or with small doses given over a period of time.

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A STUDY OF THE CONSTITUENTS IN CASCARA SAGRADA EXTRACT I. ISOLATION OF A RHAMNO-GLYCOSIDE OF EMODIN.*[1]

BY HORACE L. SIPPLE, C. G. KING AND GEORGE D. BEAL.[2]

For more than fifty years cascara sagrada extracts have been under investigation in order to determine the chemical nature of the compounds which are responsible for the characteristic cathartic properties. The extracts are usually classified as anthracene, anthraquinone or emodin cathartics, because the characteristic constituents separated have been derivatives of methyl anthraquinones. Dohme and Englehardt (1) reported finding a substance present in cascara which resembled frangulin (m. p. 237°), but their conclusion was questioned by Jowett (2). Beal and Tumminkatti (3) and Daels (4) have shown that the anthraquinone-type substances present are in part free and in part combined in a form which is liberated by hydrolysis. It is now generally accepted that the anthraquinone derivatives are present in part in a glycosidic type of linkage (5), (6). Thorpe and associates have reported finding a glycoside (frangulin) of rhamnose and emodin in Rhamnus frangula (7). Definite identification of the most active substance or substances remains to be accomplished, however. This study of the separation of the chemical constituents of cascara sagrada extract has been made to obtain further information leading toward the identification of the cathartically active constituent or constituents. A glycoside of rhamnose and emodin has been identified as one of the substances present in considerable quantity.

EXPERIMENTAL.

A procedure has been developed for the first stages of a separation of the chemical constituents in an alcoholic extract of the dry cascara bark. The various fractions thus obtained were representative of types of material present, providing a

* The authors are indebted to the Parke, Davis and Co. for a research fellowship grant (for H. L. S.), and for supplying the cascara bark.

[1] Contribution No. 276 from the Department of Chemistry, University of Pittsburgh.

[2] Assistant Director, Mellon Institute of Industrial Research.

basis for continued study of the individual compounds. The chief steps in the procedure may be summarized as follows:

1. A 300-Gm. sample of dry cascara bark was ground to approximately 10 mesh and extracted with 2 liters of 96% ethanol in a modified Soxhlet extractor for fifty hours. Extraction with ethanol rather than water prevents hydrolysis of glycosides (an undesired side reaction that would occur in an aqueous extract due to the action of accompanying enzymes), thus affording greater assurance that any products isolated would represent original constituents of the bark. The substances extracted by ethanol are chiefly water-soluble compounds. Except for a small amount of lipid material, they are precipitated from alcoholic solution upon the addition of solvents such as ethyl acetate, ethyl ether, isopropyl ether, petroleum ether, benzene or chloroform.

2. The alcoholic extract was filtered, evaporated *in vacuo* below 50° C. to approximately one-tenth of the original volume, treated with eight volumes of water and filtered.

3. The filtrate was stirred for two hours with approximately 35 Gm. of ferric hydroxide in suspension to give a clear filtrate which would not cloud when stirred with saturated NaCl solution.

4. The liquid phase from step 3 was treated with 300 cc. of a saturated solution of neutral lead acetate ($(CH_3COO)_2Pb.3H_2O$) and filtered, the small amount of precipitate formed being discarded.

5. A basic lead complex was precipitated at a p_H of approximately 7.4 (phenol red) by the addition of dilute ammonium hydroxide. The lead complex was centrifuged, the supernatant liquid decanted and discarded.

6. The lead complex was decomposed in concentrated sodium sulphate solution, the mixture being made slightly acid with acetic acid. Lead sulphate formed was removed by centrifuging and decanting the liquid phase. Reagents such as phosphoric acid, sulphuric acid and hydrogen sulphide have been avoided because of undesired side reactions which might occur.

7. The decanted liquid was evaporated *in vacuo* to 100 cc., treated with 4 volumes of methanol and filtered. Salts such as sodium sulphate, lead sulphate and some sodium acetate were precipitated. More salts, chiefly sodium acetate, were removed by evaporating the liquid to 50 cc. and filtering.

8. The liquid fraction was treated with one volume of absolute methanol, forming a brown precipitate which was centrifuged and discarded.

9. After evaporation to one-half the original volume, the liquid fraction was treated with one volume of absolute ethanol. A brown precipitate formed slowly. The mixture was allowed to stand in the refrigerator over night, centrifuged and decanted.

10. The liquid fraction, after evaporation to dryness, *in vacuo*, was taken up in 10 cc. of absolute methanol. The small amount of material not soluble in methanol was centrifuged and discarded.

11. The methyl alcohol solution was treated with five volumes of absolute acetone, causing the formation of an orange-red precipitate. The precipitate was separated in the centrifuge, washed with acetone and all liquid phases combined.

The precipitation of this acetone-insoluble material was repeated until a uniform and reproducible product was obtained. This product was then washed once with absolute acetone and dried *in vacuo* over calcium chloride. The amount of this material recovered was approximately 5 Gm. per Kg. of original bark.

12. The liquid phase from step 11 was evaporated *in vacuo* to a volume of 10 cc. and treated with ten volumes of petroleum ether, precipitating a small amount of red, oily material. A very small amount of a yellow, wax-like substance was recovered by decanting and evaporating the petroleum ether liquid phase.

The purified acetone-insoluble material obtained in step 11 did not reduce Benedict's reagent. An ether extract of an aqueous solution of the material gave no coloration with dilute ammonium hydroxide, indicating the absence of free hydroxy-methylanthraquinones (8), (9).

A 0.1-Gm. sample of the orange-red material treated with 1% HCl in a boiling water-bath for 30 minutes gave a positive test with Benedict's reagent, and an

ether extract of the hydrolyzed material treated with dilute ammonium hydroxide gave the pink coloration characteristic of a free hydroxy-methylanthraquinone.

A 2-Gm. sample dissolved in a mixture of 70 cc. of ethanol, 30 cc. of water and 6 cc. of HCl (concentrated), and heated on a boiling water-bath for eight hours gave water-soluble and water-insoluble products of hydrolysis. After dilution with three volumes of water and evaporation *in vacuo* below 50° C. in a stream of CO_2 to a volume of about 75 cc., the liquid was filtered in order to remove the water-insoluble product.

The product removed by filtration was recrystallized from glacial acetic acid and, after drying over NaOH *in vacuo*, had a melting point of 250° C. With pure emodin it gave a mixed melting point of 249° C. The pure emodin had a melting point of 251° C. It was concluded that this product of the hydrolysis was emodin.

The water-soluble fraction, after neutralization with silver carbonate and decolorization with charcoal, was evaporated *in vacuo* below 50° C. to a volume of approximately 20 cc. The specific rotation recorded was approximately +5.0.

The optical rotation of the unhydrolyzed glycoside from step 11 could not be determined readily because of the deep red color of solutions of the substance.

The phenylosazone of the water-soluble product of hydrolysis gave a melting point of 181° C., and mixed with rhamnose phenylosazone gave a melting point of 179° C. Rhamnose (Merck) gave a phenylosazone melting at 180° C.

A portion of the water-soluble fraction distilled with HCl (sp. gr. 1.06) gave a distillate that colored aniline acetate paper yellow, a test for methyl furfural (5). It was concluded that the hydrolysis product soluble in water was rhamnose, and that the compound hydrolyzed was a glycoside of rhamnose and emodin.

The recrystallized glycosidic substance (step 11) was inactive as a cathartic in doses of 120 mg. (extract from 3-Gm. bark) when given to mice. The guinea pig dose was above 300 mg. of the dry material. Pure emodin fed to mice in 5-, 10- and 20-mg. doses was also apparently inactive, although possibly slightly active at the 20-mg. level.

The minimum cathartic dose for mice of a concentrated aqueous extract of cascara sagrada was found to be equivalent to the extract from 50-mg. bark. The minimum dose per 250-Gm. guinea pig was equivalent to the extract from 300 mg. of bark.

The alcoholic extract of cascara sagrada fed to mice was active in doses equivalent to the extract from 50 mg. of bark. According to Munch (11) the approximate minimum human dosage is equivalent to the extract from 1 Gm. of bark.

SUMMARY.

A procedure has been developed for the first stages of a separation of the chemical constituents in an alcoholic extract of cascara sagrada.

A glycoside of rhamnose and emodin has been identified as one of the substances present in this alcoholic extract.

Biological tests have been made of the cathartic properties of (*a*) the rhamnose-emodin glycoside, (*b*) pure emodin, (*c*) an aqueous extract of cascara sagrada and (*d*) an alcoholic extract of cascara sagrada.

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STUDIES IN PERCOLATION.*

BY MILTON WRUBLE.

DETANNATED TINCTURE OF CINCHONA.

Tinctura Cinchonæ Detannata was official in the N. F. 1886, 1896 and 1906. The tannins were removed from the tincture as the name implies. As early as 1866, Walker (1) briefly described a method by which he prepared a fluidextract of cinchona of a beautiful red color which held the cinchotannates in solution, by percolating with diluted alcohol. Meumann, in 1886 (2), discussed the method for preparing detannated tinctures by means of ferric hydroxide. His method could be applied to any drug but was outlined for cinchona. The ferric hydroxide magma was added to the bark and intimately mixed. The mixture was transferred to a percolator and percolation allowed to proceed.

A year later, Meumann published a second paper (3) in which he recommended 2 parts of ferrous sulphate to 3 parts of bark. Remington (4), in 1887, furnished a formula for the detannated tincture according to which the U. S. P. fluidextract was treated with ferric hydroxide. In 1888, Tiarks (5) reported on the method generally employed for preparing detannated fluidextracts. He mentions the use of albumin, gelatin, lime and ferric hydroxide. Keutmann (6), in 1903, described a method for detannating cinchona by percolating a mixture of the bark with calcium hydroxide after first forming a magma of the two with water and adding ammonium carbonate. It is doubtful whether he obtained a completely detannated tincture since he reports a cherry-red color for the preparation made in this manner, whereas a completely detannated tincture is yellowish in color. However, the red color may have been due to cinchona red (not to cinchotannic acid) which is reported to be *soluble* in ammonia water.

Experimental Part.—Cinchona bark, No. 20 powder was used. When assayed according to the U. S. P. X, it yielded 4.70%, 4.32% and 4.26% of total alkaloids in as many assays. The tannin content was determined by the hide powder method (7). Three determinations yielded 4.18%, 4.17% and 4.46%, respectively.

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* Scientific Section, A. PH. A., Madison meeting, 1933.

The alkaloids of cinchona bark are supposed to be combined, in part at least, with cinchotannic acid. No therapeutic value, so far as alkaloidal action is concerned, seems to be attached to this peculiar combination (8). Inasmuch as cinchotannic acid, under certain conditions changes to cinchona red, an insoluble phlobaphene, the presence of the cinchotannic acid is supposed to be responsible for unsightly depositions in the tincture and other galenical preparations. Moreover, it has been reported that the cinchona red, as it is formed and deposited, occludes alkaloid. Hence, the formation of a deposit in the tincture is not only a cause of unsightliness, but may bring about a reduction in the alkaloidal content as well (9).

It seemed desirable, therefore, to remove the cinchotannic acid from such preparations in which this agent was not specially wanted. Instead of removing it from the tincture after the latter had been prepared, it seemed preferable to prevent its solution in the menstruum in the percolator. For this purpose calcium and ferric hydroxides might be regarded, *a priori*, as equally suitable. Moreover, either reagent would be expected to set free any alkaloids combined in the drug with cinchotannic acid, and thus possibly, aid in their solution.

DETANNATION WITH CALCIUM HYDROXIDE.

I. Enough CaO was used to yield 100 Gm. of $Ca(OH)_2$ when slaked with the theoretical amount of water. The slaked lime was mixed intimately with 100 Gm. of powdered cinchona bark, the mixture moistened with 150 cc. of alcohol and packed into a cylindrical percolator. Sufficient alcohol was added from time to time to yield 500 cc. of tincture. However, the percolate was collected in five fractions of 100 cc. each. These fractions were examined separately as was also a sixth fraction of 100 cc., *i. e.*, 100 cc. more than the formula for the preparation calls for. In the following table there will be found recorded the following data:

A. The length of time required for the percolation of each fraction.
B. The density of the percolate determined at 20° by means of a pycnometer.
C. The percentage of alcohol (by volume) ascertained by the U. S. P. X method.
D. The amount of extractive determined by the U. S. P. X method.
E. The alkaloidal content determined by the U. S. P. X assay method (U. S. P. X page 452).

	I.	II.	III.	IV.	V.	VI.
A.	10 hrs.	13 hrs.	15 2/3 hrs.	16 hrs.	15 1/2 hrs.	15 hrs.
B.	0.8359	0.8257	0.8280	0.8248	0.8195	0.8263
C.	75.60%	76.80%	81.48%	81.08%	81.08%	86.96%
D.	1.65%	0.77%	0.44%	0.14%	0.11%	0.15%
E.	1.02%[a]	0.45%[b]	0.28%[c]	0.17%[d]	0.13%[e]	0.18%[f]

[a] The average of 2 determinations, *viz.*, 1.07% and 0.97%.
[b] The average of 2 determinations, *viz.*, 0.45% and 0.45%.
[c] The average of 2 determinations, *viz.*, 0.30% and 0.26%.
[d] The average of 2 determinations, *viz.*, 0.15% and 0.18%.
[e] The average of 2 determinations, *viz.*, 0.14% and 0.11%.
[f] The average of 2 determinations, *viz.*, 0.20% and 0.16%.

The dregs were further extracted to completion with the same menstruum and the following determinations made:

Percentage extractive	1.96%
Percentage alkaloids	0.83%
Percentage tannin	0.11%

The resulting tincture was straw yellow in color. Upon standing for several months the color assumed a reddish tint. It gave no reaction with ferric chloride, hence may be assumed to have been free from tannin.

A. The period of percolation varied from 10 to 16 hours for each 100-cc. percolate.

B. With minor irregularities, the density of the five percolates constituting the tincture decreased with the extraction. In this respect the fractional percolates differ from those in which the bark was not mixed with calcium hydroxide (10). It may therefore be that, in the regular percolation, the cinchotannic acid is changed, in part at least, to an intermediate soluble product between it and the insoluble cinchona red which, on account of its greater density, causes a rise in density in the intermediate fractions.

C. Inasmuch as the alcohol used was 95 per cent by volume (not the official menstruum), it becomes apparent that the moisture of the air-dried drug was taken up, for the most part it would appear, by the strong alcohol reducing its ethanol content by about 20 per cent. From the table it also becomes apparent that the ethanol content of the percolate increased to about 81 per cent where it seemed to remain stationary so far as the official amount of percolate is concerned. But even the final percolate to approximate exhaustion, contained about 8 per cent less ethanol than the menstruum employed. It might be worth while to repeat the experiment in a dry atmosphere in order to ascertain whether the water taken up by the alcohol came from the mixture in the percolator (drug + $Ca[OH]_2$) or from the air.

D. The total extractive of the 500 cc. of tincture contained but 3.11 per cent of extractive, whereas percolate VI contained 0.15 per cent, making a total of 3.26 per cent (to this should be added the 1.96 per cent of the "exhaustive" extraction, making a total of 5.22 per cent) as compared with 20.27 per cent for the drug not treated with calcium hydroxide. Whereas the percentage of extractive decreases with each succeeding fraction of percolate, the percentages of extraction and the corresponding densities do not appear comparable. Thus for percolates II and III the corresponding figures are:

Density	0.8257	0.8280
Extractive	0.77%	0.44%

Although the density has increased slightly, the percentage of extractive has dropped materially. Again we observe some of the irregularities recorded in connection with the percolation of cinchona by itself with alcohol (11).

E. The alkaloidal content of the 500 cc. of tincture is only 2.05 per cent, percolate VI, supposed to represent more complete extraction, contained but 0.18 per cent making a total of 2.23 per cent. (Again there should be added 0.83 per cent making a total of 3.06 per cent.) The crude drug had assayed 4.42 per cent. These figures indicate a loss of more than 1 per cent. (It has been assumed that in the deposition of cinchona red from the tannin—containing tincture, alkaloid is occluded by the cinchona red formed. It may be possible that a like occlusion takes place in the percolators.) Roughly speaking the second fraction of percolate contained somewhat less than one-half as much alkaloid as the first fraction, the third fraction somewhat more than half as much as the second, the fourth somewhat more than one-half as much as the third. The fifth fraction contained not much less than the fourth, thus seeming to indicate that the last traces of alkaloid (12) still present were becoming more difficult to extract.

The $Ca(OH)_2$ must effect the solubility of substances other than the 4 + per cent of tannins, such as quinic acid, etc.

II. As in Experiment I, 100 Gm. of cinchona bark were mixed intimately with 100 Gm. of $Ca(OH)_2$ and the mixture percolated with 95 per cent alcohol until 500 cc. of tincture had been obtained. The product was of a light straw color which darkened but little upon standing. A slight whitish precipitate, presumably $CaCO_3$, resulted upon exposure to air. By way of comparison the corresponding

U. S. P. X tincture (however, 95 per cent alcohol was used) was prepared, also a third preparation using 67.5 per cent alcohol, which corresponds approximately to the menstruum of the U. S. P. X. In the last experiment the powdered cinchona bark was mixed with calcium hydroxide before it was packed in the percolator.

Some of the properties of these three tinctures are herewith tabulated:

	1. Tinct. Prepared with 95% Alc. and Lime.	2. U. S. P. Tinct.	3. Tinct. Prepared with 67.5% Alc. and Lime.
A. Time of percolation	79½ hrs.	85¾ hrs.	88½ hrs.
B. Sp. gr. 20°	0.8127	0.9302	0.9093
C. Percentage alcohol (vol.)	86.46%	68.30%	55.42%
D. Percentage of extractive	0.78% (13)	7.93%	2.10%
E. Percentage of alkaloid	0.44% (14)	1.19% (15)	0.925% (16)
F. Action upon litmus	Alkaline	Alkaline	Alkaline (17)
G. Test with $FeCl_3$	Negative	Positive	Negative

A. Whereas the periods of percolation varied as much as almost 10 hours it may be that this difference in time had no appreciable effect on the constants determined.

B. That the densities of 2 and 3, in the preparation of which a diluted alcohol had been employed, should be higher than that of 1 was to be expected. The density of 1, however, is lower than that of the corresponding tincture reported under Experiment I.

C. The ethanol content of tincture 1 is appreciably higher than that of the tincture reported under Experiment I. The ethanol content of tincture 2 is slightly higher than that of the menstruum employed, whereas that of tincture 3 is appreciably lower. It would appear, therefore, that even 67.5 per cent alcohol exerts a dehydrating effect on $Ca(OH)_2$.

Preparation of Quinic Acid.—Approximately 500 Gm. of the lime-treated dregs were extracted in a percolator with water until exhausted. The water extract was evaporated to dryness, the residue boiled with 95 per cent alcohol, and filtered. The alcohol removed material, which was of an amorphous character. The residue, insoluble in alcohol, was dissolved in warm water, decomposed with oxalic acid, the calcium oxalate filtered off and the quinic acid crystallized.

Fate of Tannic Acid in Drug.—Lime apparently removes the tannins from cinchona in the form of calcium tannate. Tannin determinations made on the dregs by means of the hide powder method, revealed little tannin. These determinations were made by first treating the bark with HCl so as to free the tannin.

Qualitative tests for tannins were made with ferric chloride and gelatin solution after first treating the bark with acid as stated above. No tests for tannins were apparent. The solutions were then carefully neutralized with ammonia and the tests with ferric chloride and gelatin repeated with the same results.

Further attempts were made to learn of the function of the lime in the detannation of the cinchona bark. After treating the dregs with HCl and filtering the aqueous solution, it was refluxed for 4 hours. For comparison a decoction of cinchona bark was filtered, the same quantity of HCl added and refluxed in the same manner. In the case of the bark, cinchona red was obtained and identified by precipitation as the barium compound, but in the case of the detannated dregs no cinchona red was obtained. The experiment in the latter case was repeated without treating the dregs with HCl and the same results were obtained.

PREPARATION OF TINCTURE OF CINCHONA U. S. P. X, AND DETANNATED TINCTURE OF CINCHONA.

III. A liter of each of the tinctures was prepared from red cinchona bark (18) which assayed 6.37 per cent and 6.82 per cent (19), respectively, of total alkaloids (20) in as many assays by the U. S. P. X method.

The following data were determined on each tincture employing the methods as outlined in the U. S. P. X.

	U. S. P. Tincture.	Detannated Tincture (21).
Sp. gr. 20°	0.9125	0.8928
Extractive	32.30%	2.03%
Alkaloids	1.15% (22)	1.01% (23)
Test with $FeCl_3$	Tannins present	No tannins present

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(1) *Am. J. Pharm.*, 38 (1866), 411.
(2) *Pharm. Rund.*, 4 (1886), 197. (3) *Ibid.*, 4 (1886), 270.
(4) *Drugg. Circ.*, 3 (1887), 102.
(5) *Pharm. Rund.*, 6 (1888), 160.
(6) *Suedd. Apoth.-Ztg.* (1903); from *Pharm. Ztg.*, 48 (1903), 823.
(7) Villavecchia, "Applied Analytical Chemistry," 2 (1918), 338.
(8) "The properties and uses of cinchona correspond, proportionally in its strength with those of the following alkaloids (quinine, quinidine, cinchonine, cinchonidine). The cinchotannic acid being sufficient to impart astringency that is wanting in the alkaloids," Rusby, Bliss, Ballard, "Properties and Uses of Drugs," page 440.
(9) "While the precipitate consists largely of inert material, yet it carries down with it some of the active alkaloids and so weakens the preparation." Scoville, *Proc. Tercentenary of Cinchona* (1931), 214.
(10) Jour. A. Ph. A., 22 (1933), 641. (11) *Ibid.*
(12) Solubility of cinchona alkaloids at 25°.

1 Gm. quinine dissolves in 0.8 cc. ethyl alcohol.
1 Gm. quinidine dissolves in 32 cc. ethyl alcohol.
1 Gm. cinchonine dissolves in 120 cc. ethyl alcohol.
1 Gm. cinchonidine dissolves in 20 cc. ethyl alcohol.
(Merck's Index, 4th Edition.)

(13) The total extractive of the five fractions was 3.11 per cent. (See I.)
(14) Two assays gave the same results.
(15) No. 1—1.12%; No. 2—1.26%.
(16) No. 1—0.92%; No. 2—0.93%.
(17) This was more alkaline than 1.
(18) The tannin content of this bark was 2.3% and 2.5%, respectively, in as many assays, Villavecchia, "Applied Analytical Chemistry," 2 (1918), 338. The dregs showed a content of 0.31% and 0.42% tannins in as many assays.
(19) This corresponds to an average total alkaloidal content of 13.19 Gm. in the 200 Gm. of cinchona used in the percolation.
(20) Alkaloidal content of lime-treated dregs—0.37%. Alkaloidal content of U. S. P. X dregs—0.09%.
(21) This was prepared by the use of an excess of calcium hydroxide, mixed intimately with the bark and percolated. This tincture proved to be far more palatable than the U. S. P. X tincture.
(22) The average of three assays, *viz.:* 1.16%, 1.22% and 1.09%, respectively. The alkaloidal content of the liter of tincture is 11.50 Gm.
(23) The average of three assays, *viz.:* 1.02%, 0.99% and 1.03%, respectively. The total alkaloidal content of the liter of tincture is 10.10 Gm.

PHYSICS IN PHARMACY.

Part V, A Strip of Filter Paper or Capillary Hydrostatics, Capillary Diffusion and Capillary Osmosis.*,[1]

BY JOHN URI LLOYD, WOLFGANG OSTWALD AND HANS ERBRING.

I. PRESENTATION AND THEORY.

1. Basic Experiment.—About 35 years ago, the senior author, in a publication not easily accessible to physico-chemical investigators,[2] described the following experiment:

Connect two glass tubes closed below, one being filled with a salt solution, the other with water, by means of a strip of filter paper, and bring the meniscuses in

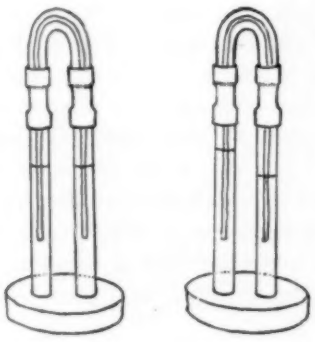

Fig. 1*a*.

Fig. 1*b*.

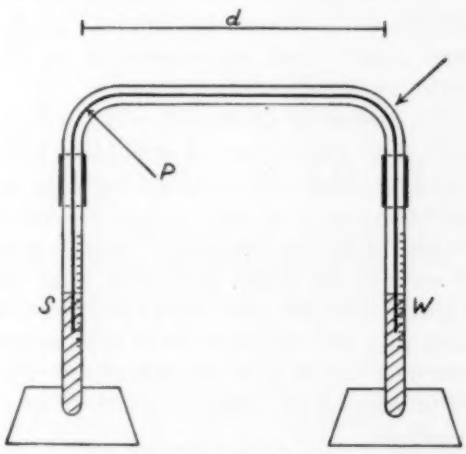

Fig. 2.—S, Salt solution; W, Water; P, Filter paper.

both tubes to the same level by raising or lowering the tubes (see *Fig. 1a*, original figure). Protect the system from evaporation by means of a connecting tube bent in U shape and two short pieces of rubber tubing.

After a few hours, more plainly after a few days, it is found that a motion of the liquid has taken place. The liquid column in the tube with the salt solution has increased, that in the tube containing water has diminished. Hence, water has passed through the strip of filter paper into the salt solution (see *Fig. 1b*, original figure).

The experiment looks very simple; its explanation, however, is not correspondingly simple. We shall see in the following study that in this apparently "spontaneous" transport of liquid, quite a series of physico-chemical principles is involved which should be of interest to the thoughtful pharmacist. In the following pages, we have taken up the problem of determining the nature of these forces in order to find an explanation of this effect.

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* Translated from the German by Dr. Sigmund Waldbott.

[1] Scientific Section, A. Ph. A., Toronto meeting, 1932.

[2] John Uri Lloyd, "Etidorpha," The Robert Clarke Company, 1897, page 138.

It is evident that if this phenomenon can be seen to rest on a safe experimental and possibly also theoretical basis, it will be of interest in many a question of physical and colloid chemistry. The senior author himself (*loc. cit.*) has pointed out that such movements of liquids would affect geological and hydrological questions, *e. g.*, as to the origin of salt lakes and subterranean water courses, thereby assuming that porous materials like sand, sandstone, etc., act in the same manner as filter paper. Then the theories of "swelling" suggest themselves. Concerning this, different authors, *e. g.*, Proctor and Wilson, J. Duclaux, D. Jordan Lloyd, J. Loeb, Northrop and Kunitz, etc., have recently considered "osmotic" forces in the movement of water in the swelling of gels although the existence of "cell structure" or "semipermeable membrane" in swelling gels has not always been proved, nor is it even always considered probable.

In filter paper, also, we have movement of water without cell- or (honey) comb structure, and without membranes. Such movements of liquids "without membranes" might be of importance also in the physiological problems of movements of water in the organism.

2. Method of Operation.—The following method was used in these experiments. Two glass tubes, closed at one end, each 10 cm. long and of 0.5-cm. diameter, and provided with a millimeter scale, were filled to about $^3/_4$ with the solutions to be examined, and placed upon a suitable support. Through a U-shaped glass tube, also of 0.5-cm. diameter, a thin strip of filter paper, 2–3 mm. wide, was drawn, both ends of the paper projecting from the tube. The two strips of paper were introduced into the two liquid cylinders, immersed to a definite distance in the liquids, and two short pieces of rubber attached to the ends of the U tube were drawn over the edge of the cylinders. The pieces of rubber were covered with a layer of paraffin or "pizein," which protected the system quite well from loss by evaporation.

The resulting arrangement is represented in *Fig. 2*. In all experiments, the paper was immersed in the liquid to a depth of 3 cm. The filter paper was used, either dry or moistened with the solutions employed. For an account of the differences noted, see *Section 5*. Also, different grades of filter paper have been used; see *Section 6*. At the beginning of the experiment, the meniscuses must be exactly at the same height in both cylinders; this is easily attained by vertical change of position of the cylinders.

It is furthermore important that the connecting piece *d* shall always be in an exactly horizontal position.

The changes in the position of the meniscuses were read at both scales by means of the lens. The experiments were carried out at ordinary room temperature, since it was found that the use of thermostats was superfluous as the temperature factor proved to be very insignificant. Cf. *Section 10*.

3. Repeating the Basic Experiment.—The following is an example taken at random from the many experiments which we conducted according to the above method, in order to demonstrate that the basic experiment is reproducible, and at the same time to characterize the Effect quantitatively.

Table I shows an experiment with saturated *ferric chloride* solution. The length of the horizontal connecting piece was 9 cm. (see *d* in Fig. 2). In this experiment the filter paper was used *dry*. Upon connecting the two liquids by the filter paper, there is at first capillary rise in

both tubes; in this case, salt solution and water meet on the side of the salt solution. It was only after this capillary connection was completed that the leveling of both liquid surfaces was done.

TABLE I.

System: $FeCl_3$ (saturated) *vs.* Water. d = 9 cm.

1. Duration of Exp., Hours.	2. Height in Cyl. S, Cm.	3. $FeCl_3$ Increase in Cyl. S, Mm.	4. Height in Cyl. w, Cm.	5. H_2O Decrease in Cyl. w, Mm.	6. Total Difference, Mm.	7. Liquid Taken Up by Paper; Col. 5 Minus Col. 3, Mm.
0	5.00	0.0	5.00	0.0	0.0	0.0
16	5.1	1.0	4.65	3.5	4.5	2.5
42	5 15	1.5	4.5	5.0	6.5	3.5
62	5.22	2.2	4.35	6.5	8.7	4.3
80	5.25	2.5	4.33	6.7	9.2	4.2
100	5.3	3.0	4.25	7.5	10.5	4.5
Days.						
8	5.35	3.5	4.15	8.5	12.0	5.0
11	5.35	3.5	4.15	8.5	12.0	5.0
14	5.35	3.5	4.15	8.5	12.0	5.0
16	5.35	3.5	4.2	8.0	11.5	4.5
20	5.3	3.0	4.25	7.5	10.5	4.5
25	5.28	2.8	4.3	7.0	9.8	4.2
40	5.2	2.0	4.35	6.5	8.5	4.5

The headings of the 7 columns in Table I are self-explanatory; the results, also represented graphically, in Figs. 3 and 4, furnish a quantitative characterization of the effect.

From *Table I* and the *diagrams*, the following results are noteworthy.

1. The principal effect takes place within about the first 8 days.
2. Upon longer duration of the experiment, the effect again decreases, the movement of the liquid becomes retrograde; however, the descent takes place more slowly than the rise.
3. The decrease in the cylinder containing water runs somewhat parallel to the increase in the salt solution, but is of much higher absolute value than the latter.

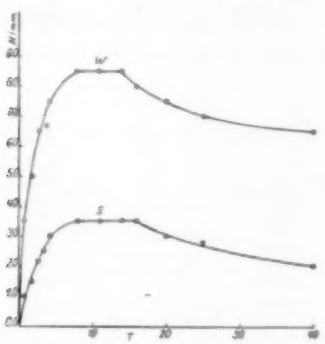

Fig. 3.—N, Difference of level in mm.; T, Time in days. Curve W shows decrease in the water cylinder; Curve S shows increase in the salt cylinder.

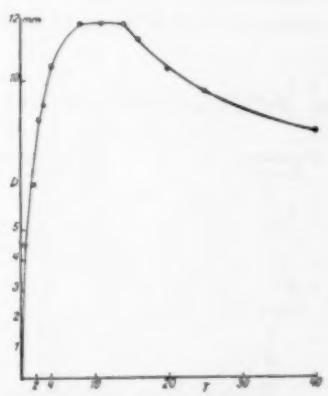

Fig. 4.—D, Total difference; T, Time in days.

A considerable quantity of the liquid "disappears" in the experiment; this is especially noticeable in *Fig. 3*. The "vanished" liquid is contained partly in the capillary spaces of the paper and contributes in part to the swelling of the filter

paper; another part is condensed in the form of droplets along the glass walls, especially that of the U tube.

The general course of the Effect may be well visualized by the aid of *Fig. 5*, in which the height of the liquid columns attained in the time periods I, II, III and IV are brought out by hatched lines.

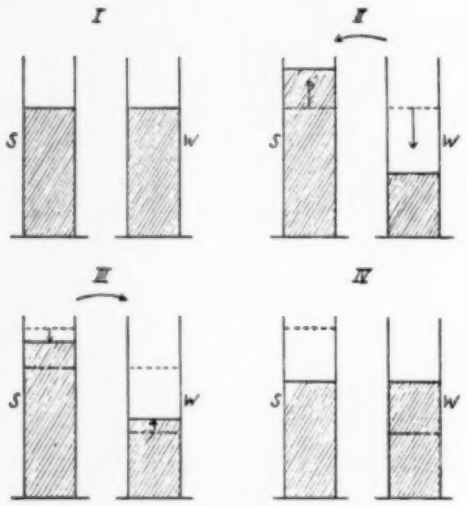

Fig. 5.

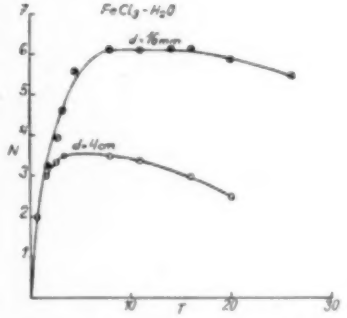

Fig. 6.—N, Increase of level in mm.; T, Time in days.

As one might be inclined to regard the numerical value of the Effect, in this case a maximum difference of 12 mm. as insignificant, we present herewith in *Table II* an example to show how large an effect may be attained under certain conditions. By merely leaving $FeCl_3$ in contact with undissolved $FeCl_3$ at the bottom of cylinder S, and conducting the experiment as before, there will be, during the same period of time, differences of level of at least 28.3 mm., the maximum not yet being reached.

TABLE II.

System: $FeCl_3$ plus undissolved $FeCl_3$ at the bottom, *vs.* Water. d = 12 cm. Paper wetted at start.

Duration, Hours.	$FeCl_3$—Increase, Mm.	H_2O—Decrease, Mm.	Total Difference, Mm.
2	1.0	3.0	4.0
10	5.0	7.0	12.0
18	7.0	9.0	16.0
24	9.0	11.5	20.5
Days.			
2	10.5	14.5	25.0
4	10.5	15.5	26.0
8	11.5	15.5	27.0
15	12.5	15.8	28.3

II. FURTHER EXPERIMENTAL DETAILS.

Before passing on to the theory of the phenomenon, we wish to give from our large and varied experimental material a few experimental details in order that the effect herein considered may be viewed from other angles.

4. Influence of Length of the Capillary Connecting Piece.—In the foregoing discussion, the capillary connecting piece, *i. e.*, the strip of filter paper, is of essential importance. It therefore became of interest to know in what manner the dimensions, particularly the length (*d*) influences the Effect. Summing up, we find a dis-

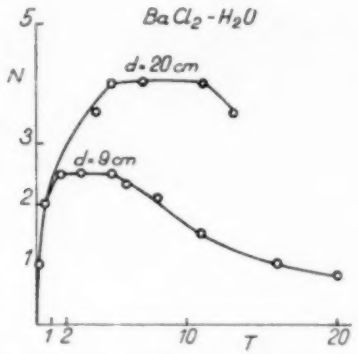

Fig. 7.—N, Increase of level in mm.; T, Time in days.

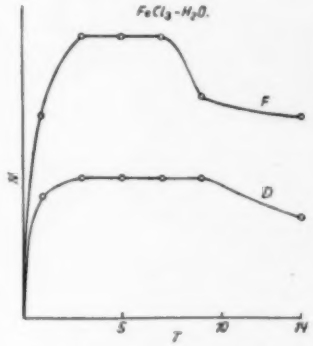

Fig. 8.—N, Increase of level in mm.; T, Time in days; F, Moist; D, Dry.

tinct *increase of the Effect with increase of length, provided*, however, that the *paper is previously moistened with the solution.* Experimental details for this are given in the following *Tables III, IV, V, VI,* and *Figs. 6* and *7;* salt solutions used against water were saturated *Ferric Chloride* and saturated *Barium Chloride* solutions.

TABLE III.—INFLUENCE OF LENGTH OF *d* (*d* = 4 CM.).

System: $FeCl_3$ (saturated), *vs.* Water. Paper moistened with $FeCl_3$ at start.

Duration, Hours.	$FeCl_3$—Increase, Mm.	H_2O—Decrease, Mm.	Total Difference, Mm.	Liquid Taken Up by Paper, Mm.
16	2.0	4.0	6.0	2.0
42	3.0	8.0	11.0	5.0
62	3.3	8.5	11.8	5.2
80	3.5	8.5	12.0	5.0
100	3.5	8.5	12.0	5.0
Days.				
8	3.5	8.0	11.5	4.5
11	3.5	7.5	10.8	4.2
16	3.0	7.5	10.5	4.5
20	2.5	7.3	9.8	4.8

TABLE IV.

Same as Table III, except *d* = 16 cm. Paper moistened at the start.

Duration, Hours.	$FeCl_3$—Increase, Mm.	H_2O—Decrease, Mm.	Total Difference, Mm.	Liquid Taken Up by Paper, Mm.
48	3.2	8.0	11.2	4.8
66	3.9	10.0	13.9	6.1
80	4.6	12.0	16.6	7.4
110	5.6	13.5	19.1	7.9

Days.				
8	6.1	14.0	20.1	7.9
11	6.1	14.0	20.1	7.9
14	6.2	14.0	20.2	7.8
16	6.2	14.0	20.2	7.8
20	5.9	13.8	19.7	7.9
30	5.5	13.4	18.9	7.9

TABLE V.—INFLUENCE OF LENGTH OF d (d = 9 CM.)

System: $BaCl_2$ (saturated), *vs.* Water. Paper moistened with $BaCl_2$ at start.

Duration, Hours.	$BaCl_2$—Increase, Mm.	H_2O—Decrease, Mm.	Total Difference, Mm.	Liquid Retained by Paper, Mm.
8	1.0	1.7	2.7	0.7
16	2.0	3.0	5.0	1.0
42	2.5	4.0	6.5	1.5
Days.				
3	2.5	5.0	7.5	2.5
4	2.5	5.0	7.5	2.5
5	2.5	5.0	7.5	2.5
6	2.3	5.0	7.3	2.7
8	2.1	5.0	7.1	2.9
11	1.5	5.0	6.5	3.5
13	1.5	5.0	6.5	3.5
16	1.0	4.8	5.8	3.7
20	0.7	4.6	5.3	3.9

TABLE VI.—INFLUENCE OF LENGTH OF d (d = 20 CM.)

System: Same as in Table V. Paper moistened at start.

Duration, Hours.	$BaCl_2$—Increase, Mm.	H_2O—Decrease, Mm.	Total Difference, Mm.
22	2.0	2.2	4.2
Days.			
4	3.5	4.0	7.5
5	4.0	5.0	9.0
7	4.0	6.0	10.0
11	4.0	6.0	10.0
13	3.5	6.0	9.5

With $FeCl_3$ (*Tables III* and *IV*), we see that the fourfold length of the capillary connecting piece results in practically doubling the Effect (increase of level in cylinder S). Relatively still more pronounced is the Effect with $BaCl_2$ (*Tables V* and *VI*), where tubes with d = 9 cm. and 20 cm. are used.

In both cases, we also note a faster decline from the maximum in the shorter connecting tube. Experiments with still longer tubes have shown that the errors caused by the large quantities of the liquid retained by the paper and by condensation of liquid become so great as to render results inexact; hence longer connecting tubes cannot be recommended.

5. Influence of Preliminary Wetting.—In starting the experiment, we may allow both liquids to rise and meet in the dry paper, or we may first moisten the paper with the salt solution, then continue with the experiment. Moistening with water would practically have the same effect as the use of dry paper, since water

as a rule rises very much faster than the solution; in this case, both liquids would meet in cylinder S.

We found the Effect to be notably stronger and better reproducible if the solution is allowed to migrate into the filter paper, as high as into the beginning of the descending branch of the connecting tube on the water side (see arrow in *Fig. 2*). Waiving numerical data for this experiment, we show in *Fig. 8* the graphic results of such a parallel experiment with wet and with dry filter paper.

6. Influence of the Quality of Paper.—Filter papers are usually characterized by their transversal permeability, *i. e.*, according to the average diameter of their pores. A paper with very small-sized pores is, *e. g.*, that of Schleicher and Schüll No. 602 (hard); the size of pores is about 2.2μ.[1] Again, filter papers may be characterized by their "imbibing ability," *i. e.*, by the speed of capillary rise of water in them. This is a longitudinal property of the paper, caused by an especially numerous aggregation of narrow capillaries. Such a paper is that of Schleicher and Schüll No. 604 (soft); it has considerably larger transversal pores than the hard paper No. 602. The paper used in the preceding experiments was intermediate between these two extremes.

TABLE VII.—INFLUENCE OF QUALITY OF PAPER. PAPER WETTED AT START.

System: $FeCl_3$ (saturated), *vs.* Water. d = 12 cm.

Duration, Hours.	$FeCl_3$—Increase, Mm.	H_2O—Decrease, Mm.	Total Difference, Mm.	Liquid Retained by Paper, Mm.
		Paper No. 604 (Soft).		
22	5.0	8.5	13.5	3.5
70	7.0	10.5	17.5	3.5
Days.				
5	7.0	10.5	17.5	3.5
7	7.0	13.0	20.0	6.0
9	5.5	16.0	21.5	10.5
14	5.0	18.5	23.5	13.5
Weeks.				
8	2.0	16.0	18.0	14.0
		Paper No. 602 (Hard).		
Hours.				
70	1.0	4.0	5.0	3.0
Days.				
5	1.5	6.5	8.0	5.0
7	2.5	7.5	10.0	5.0
9	3.5	8.5	12.0	5.0
14	3.0	8.5	11.5	5.5
Weeks.				
8	1.5	7.5	9.0	6.0

Table VII and *Fig. 9* show considerable difference existing in the activity of the soft, felt-like paper, compared with that of the hard and dense paper No. 602. The Effect is of much greater magnitude with the former than with the latter. With No. 604, the maximal increases of level are more than twice as much as with

[1] Cf. Wo. Ostwald, "Kleines Praktikum der Kolloidchemie," 7th Edition, page 26 (Steinkopff, Dresden).

No. 602. The kinetics of rise are likewise different; with No. 604, the rise takes place far much faster than with No. 602.

There is also a notable and plausible difference in the quantities of liquid retained in the filter paper; cf. the last column in *Table VII*.

7. *Clogging of the Capillaries by Formation of a Precipitate.*—In a systematic study on the relation of size of pores in unglazed porcelain and osmotic activity by *L. Bigelow* and *F. E. Bartell* (see later), Bartell found, for example, that porcelain

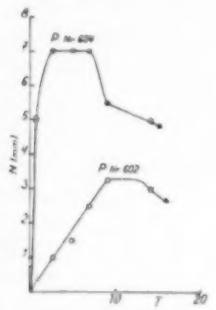

Fig. 9.—N, Increase of level in mm.; T, Time in days; P, Filter paper.

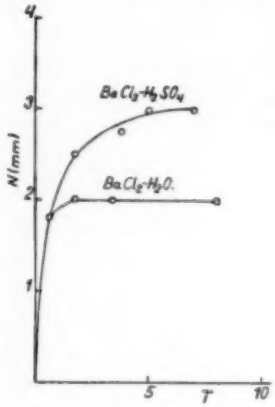

Fig. 10.—N, Increase of level in mm.; T, Time in days.

with pores smaller than 0.4μ is of direct use as an osmotic cell. He also diminished the width of the pores by precipitating $BaSO_4$, S, $PbCrO_4$, CuS, etc., within the capillaries of the pores; this likewise caused an increase of the capillary effect.

Although a piece of filter paper longitudinally soaked with liquid is evidently different from a transversally soaked wall of a porcelain cell, we may believe that in both cases a narrowing of the capillaries, resp., the pores will act in the same direction. Accordingly we have also tried to diminish the width of the fibrillary capillary spaces by depositing within them finely divided precipitates.

TABLE VIII.

System A: $BaCl_2$ (saturated) *vs.* Water. d = 4 cm. Paper dry at the start.

Duration, Hours.	$BaCl_2$—Increase, Mm.	H_2O—Decrease, Mm.	Total Difference, Mm.
16	1.8	2.5	4.3
42	2.0	3.5	5.5
62	2.0	4.0	6.0
80	2.0	4.5	6.5
Days.			
8	2.0	5.0	7.0

Now Clogging the Capillaries by Precipitation.

System B: $BaCl_2$ (saturated), *vs.* 0.1N H_2SO_4. d = 4 cm.

Hours.	Mm.	Mm.	Mm.
16	1.8	2.8	4.6
42	2.5	3.5	6.0
90	2.5	4.5	7.0

Days.			
5	3.0	5.0	8.0
7	3.0	5.2	8.2

In *Table VIII* and *Fig. 10* are shown the results of an experiment (*System B*), in which the capillary spaces are diminished in size by precipitation of $BaSO_4$ within them; water placed against the saturated $BaCl_2$ solution in *System A* is substituted by tenth-normal sulphuric acid.

The narrowing of the capillary tubes is seen to result in the increase of our Effect.

8. Experiments with Other Substances.—The experiments described thus far were carried out with $FeCl_3$ and $BaCl_2$ *vs.* water. Without presenting numerical values, we see from *Figs. 11* and *12* that the effect is obtained also with *KCl* (univalence) and with $AlCl_3$ (trivalence), and with non-electrolytes such as *Cane sugar*.

Experiments we carried out with *Urea* will be described in *Section 10.*[1]

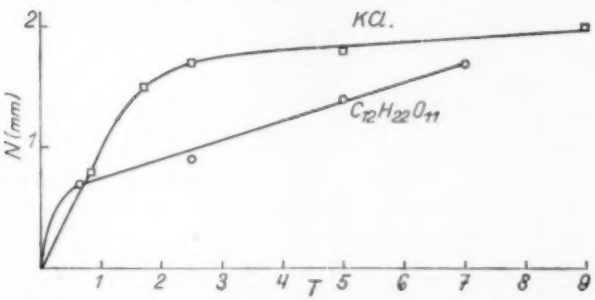

Fig. 11.—N, Increase of level in mm.; T, Time in days; Paper dry at start.

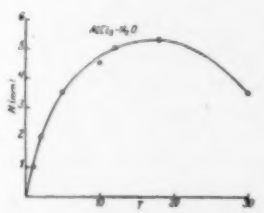

Fig. 12.—N, Increase of level in mm.; T, Time in days; Paper wet at start.

It might appear strange that cane sugar gives but a relatively small Effect as compared with that of the salts. However, when comparing the curves in *Fig. 11*, we see that only the *beginning* of the curve of the sugar has been measured, while the KCl curve, after about 8 days, runs practically horizontal, the curve for the sugar, during the same time, shows a decided, almost linear rise. The thought suggests itself to hold the high molecular weight of the sugar, and the high viscosity of its solutions responsible for the smaller velocity displayed in producing the Effect. In addition, this experiment with cane sugar was conducted at the time when the importance of preliminary wetting had not yet been recognized.

9. Quantities of Liquids Retained by the Filter Paper.—In the first part of this paper, attention was called to the relatively large quantities of liquid held by the filter paper. These quantities vary, not only according to the kind of filter paper used (cf. *Section 6*), but also according to the nature of the solution.

(End of First Instalment.)

[1] Alcohols used in the experimental apparatus herein described, showed *peculiar movements*, concerning which we shall report in a later communication.

Eighty-second annual meeting of AMERICAN PHARMACEUTICAL ASSOCIATION and dedication of the American Institute of Pharmacy during week of May 7th. See Transportation under department "Societies and Colleges."

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THE REPUTED INFLUENCE OF ULTRAVIOLET LIGHT ON THE YIELD OF DIGITALIS GLUCOSIDES.*

BY C. S. LEONARD AND JOHN M. ARTHUR.

It has been claimed that the yield of active drug substances in certain drug plants can be altered by differences in the quality of the light under which they are grown. Thus, McCrea (1) has claimed that if seedlings of *Digitalis purpurea* are sprouted and grown for a time under a glass having a high ultraviolet transmission, then set into the field, dried powdered leaf made from these seedlings will yield more cardiac glucosides, as tested by bioassay than will that from similar plants sprouted under window glass and set out into the field.

In examining this work it appeared to the writers that a number of factors were not controlled in Miss McCrea's experiments and that some of these factors could be kept constant during the experimental period with the facilities available at the Boyce-Thompson Institute. The experiments here reported have been in progress for three years. Two strains of seed of *Digitalis purpurea* were obtained, one from Professor Edward Kremers of the University of Wisconsin and grown at the Pharmaceutical Experiment Station there, the other was obtained from a local seedman of the New York district (called Vaughan's strain). Both species were germinated and grown under the standard conditions possible in two air-conditioned greenhouses of the Boyce-Thompson Institute, but one group of each was under "Sunlit" glass with which one greenhouse is glazed, the other under ordinary window glass. The "Sunlit" glass used varied in thickness from 2.5 to 3 mm. Coblentz and Stair (2) found an average transmission for "Sunlit" glass at wave-length 302 mμ of 65% when new and 39% after solarization by exposure to a mercury vapor

* Contribution from the Burroughs Wellcome and Company Experimental Research Laboratories, Tuckahoe, N. Y., and from the Boyce-Thompson Institute for Plant Research, Inc., Yonkers, N. Y.

arc. The average thickness of the samples tested was 2.3 mm. Similarly, the figures determined for "Vita" glass for like wave-length and thickness were 48% and 22%, respectively. Coblentz and Stair have pointed out that a variation in thickness of 0.1 mm. produced a change in transmission of 1.2% at a wave-length of 302 mμ. The limit of transmission of the window glass is 313 mμ. No difference of morphology of the plants (size, etc.) has been seen.

I. EXPERIMENTS IN WHICH THE PLANTS WERE KEPT FOR THREE TO FOUR MONTHS AFTER GERMINATION IN THE EXPERIMENTAL GREENHOUSES AND WERE NOT SET INTO THE OPEN.

One strain was started July 29, 1930 (Vaughan's), the other in September (Wisconsin), hence the two sets of plants were not of identical age at the time of sampling. On January 12, 1931, six sturdy plants were selected at random from each group for each powder, two powders being made from each group. All but one were dried under the same conditions in the attic of the Boyce-Thompson Institute. One was dried in an electric oven at about 45° C. Eight powders and tinctures were made by the U. S. P. method.[1] A table below gives the results.

TABLE I.—REPORT OF ASSAY BY THE U. S. P. ONE-HOUR FROG METHOD OF TINCTURES MADE FROM DIGITALIS LEAF FROM PLANTS 4–6 MONTHS IN THE GREENHOUSE.

Tincture Number.	Per Cent U. S. P.	Total Solids, Gm. per 100 cc.	Variety.	Greenhouse.	Age, Months.
1	126 ± 10*	4.06	Wisconsin	Window glass	4
2	120 ± 10*	4.11	Wisconsin	Window glass	4
3	200 ± 10*	3.26	Vaughan	Window glass	6
4	150 ± 10*	3.17	Vaughan	Window glass	6
5	109 ± 10*	3.75	Wisconsin	"Sunlit" glass	4
6	150 ± 10*	3.78	Wisconsin	"Sunlit" glass	4
7	150 ± 10*	3.08	Vaughan	"Sunlit" glass	6
8	133 ± 10*	3.20	Vaughan	"Sunlit" glass	6

* Probable error in U. S. P. bioassay (A. O. A. C.).

Comments on Table I.—Three Wisconsin samples were low in bioassay, one high. Three Vaughan samples were high in bioassay, one low. The average for the Vaughan samples is higher than the Wisconsin samples but the plants are several months older so this is to be expected. The average bioassay for the samples from both sources grown under window glass (149%) is higher than that for those grown under the "Sunlit" glass (135%). Hence, any conclusion from this would be that the extreme ultraviolet region is detrimental to the yield of alkaloids. However, as the error of bioassay is ±10%, and there is an additional slight error due to possible variations of extraction, and to the individual variations, which despite the presence of six plants in each powder, were likely to be evident, we believe that the difference seen, namely, 14% U. S. P., is within the possible error of the experiment.

II. EXPERIMENTS IN WHICH THE PLANTS WERE GROWN 4 MONTHS IN THE GREENHOUSES AND SET OUT INTO THE FIELD FOR 5 MONTHS.

The Wisconsin strain only was used. The seed was planted in January. These plants were kept in the greenhouses under the same conditions as in the first experiment. On removal to the open field a part were put into a plot of ground at the Boyce-Thompson Institute, a part at another plot located at the U. S. A.

[1] Type Process P of the U. S. P. X without the modification for the adjustment to U. S. P. strength of assayed tinctures, but rather making directly to 1000 cc.

Works of Burroughs Wellcome & Co., Inc., both in Yonkers, N. Y. A set of six sturdy plants was taken from each field and each group (previously under ordinary glass and previously under "Sunlit" glass). They were dried by spreading on a paper in an attic as before. Four powders and tinctures were made by the U. S. P. method and assayed by the U. S. P. one-hour frog method. The results are given in Table II.

TABLE II.

Tincture Number.	Per Cent U. S. P.	Total Solids, Gm. per 100 cc.	Field.	Greenhouse.	Age, Months.
9	140 ± 10	2.20	B. W. & Co.	Window glass	9
10	84	2.34	B. W. & Co.	"Sunlit" glass	9
11	84	2.70	Boyce-Thompson	Window glass	9
12	70	2.24	Boyce-Thompson	"Sunlit" glass	9

Comments on Table II.—The results tend to be lower than in the previous test, apparently because of the time of sampling. Those specimens originally under window glass were up to 70% U. S. P. higher in potency by bioassay than specimens otherwise of similar history, but originally under "Sunlit" glass. In different fields the variation in specimens of identical history is evident. This variation is from 14% to 56% U. S. P. The evidence thus afforded that the glucoside yield varies enormously with soil conditions seems significant.

III. EXPERIMENTS IN WHICH THE PLANTS WERE GROWN 9 MONTHS IN THE GREENHOUSE AND NOT SET INTO THE FIELD.

A portion of the seedlings of Experiment II were not set out into the field but were continued for the nine months in the air-conditioned greenhouses. Two sets of 6 sturdy plants were taken from each group. They were dried as before. Four powders and tinctures were made by the U. S. P. method and assayed by the U. S. P. one-hour frog method. The results are given in Table III.

TABLE III.

Tincture Number.	Per Cent U. S. P.	Total Solids, Gm. per 100 cc.	Greenhouse.	Age, Months.
13	60 ± 10	3.40	Window glass	9
14	84	3.34	Window glass	9
15	112	3.22	"Sunlit" glass	9
16	76	2.96	"Sunlit" glass	9

Comments on Table III.—The specimens grown throughout in the greenhouse also show considerable variability although here set in the same soil and kept under the same conditions as regards all factors but light. The difference in the same greenhouse of two specimens is 36% U. S. P. in the case of the specimens under "Sunlit" glass and 24% in the case of the ordinary glass. The average of the former is 94%, the average of the latter is 72%. Thus, here the specimens under "Sunlit" glass are higher in glucoside yield by 22% U. S. P. if the averages are compared, but the differences between specimens of identical history is greater (24–36% U. S. P.) and if the 84% specimen from the greenhouse with ordinary glass were compared with the 76% specimen from the house with "Sunlit" glass, the former would appear to have the advantage.

IV. EXPERIMENTS IN WHICH THE PLANTS WERE GROWN IN THE GREENHOUSES FOR 8 MONTHS, SET INTO THE FIELD OVER THE WINTER AND HARVESTED JUST BEFORE FLOWERING TIME.

As the plants grown in the previous experiments had no cold dormant period, they failed to send up flower stalks and flower. The objection might be raised that

these plants were abnormal because they did not flower. The time specified in the pharmacopœias for harvest of digitalis is just before the flowering time. Seedlings of the Wisconsin strain were grown therefore in the greenhouse for 8 months. They were germinated in January, repotted once and set out in October into two fields, one at the Boyce-Thompson Institute experimental ground and the other at the Works of Burroughs Wellcome and Company. After the usual winter dormant period of these perennials, many plants produced abundant and vigorous foliage the following spring and sent up the usual flower stalk in May. They were harvested May 27th, over 17 months after germination and after 8 months of life in the greenhouses and 9 months in the field. Six specimens were collected, 2 sets of 6 sturdy plants from the Boyce-Thompson plants of each group and one set from each group grown at the Burroughs Wellcome field. The results are given in Table IV.

TABLE IV.

Tincture Number.	Per Cent U. S. P.	Total Solids, Gm. per 100 cc.	Field.	Greenhouse.
17	104 ± 10	2.20	Boyce-Thompson	Window glass
18	74	2.27	Boyce-Thompson	"Sunlit" glass
19	61	2.20	Boyce-Thompson	Window glass
20	95	2.36	Boyce-Thompson	"Sunlit" glass
21	87	2.43	B. W. & Co.	Window glass
22	77	2.44	B. W. & Co.	"Sunlit" glass

A specimen from plants similarly treated except grown under window glass of unknown light transmitting power gave a potency of 114% U. S. P.

Comment on Table IV.—It is evident from comparing this group to Group I that the yield of active glucosides is greater in dried powdered leaf from young plants, 6 months of age, than from older plants whether these are about to flower or not. The young plants display average yields nearly double that of the older. This agrees with the observation of Miss McCrea (3). For the plants of pharmacopœial standard age (flowering time) the average of the specimens under window glass is 84%, that of the specimens under "Sunlit" glass is 82%. The difference is negligible, far within the error of the experiment.

DISCUSSION.

Finally, we may average and compare all the results of each type obtained in the four experiments on the total of 22 specimen tinctures made from the specimens, 11 with a history at least as seedlings of growth with no ultraviolet light, 11 supplied with ultraviolet light. The specimens under window glass average 110.4%, the specimens under "Sunlit" glass average 102%. This difference is about 8% U. S. P. and is well within the error of bioassay and hence it is not believed that the difference is significant, particularly in view of the wider variations which are to be seen in specimens of identical history. For example, specimens 17 and 19 are two lots of the same sort of specimens. They show 33% U. S. P. difference. Numbers 15 and 16 similarly are comparable and show 36% U. S. P. difference. Only in the experiments of Group III were the specimens under "Sunlit" glass higher than the specimens under window glass and then less than the above 36%. No consistent, significant differences were found in yield of glucosides as were found by McCrea. The above experiments demonstrate the great variation in glucoside yield which can be seen in sets of plants of identical prior history set into different fields or even from different regions of the same field. Even when

grown in pots, with a presumably uniform soil and kept under controlled and constant greenhouse conditions, two lots of 6 plants each, both under "Sunlit" glass, show as much as 36% U. S. P. variation. The averages obtained in the experiments here reported do not permit any assumption that the influence of the extreme ultraviolet region of sunlight, either during the seedling stage or throughout the life of the plant, affects the yield of active glucosides.

SUMMARY.

No significant differences in glucoside yield could be observed between digitalis plants grown under a glass having a higher ultraviolet transmission and those grown under ordinary window glass, whether the plants were kept until sampled in the air-conditioned greenhouses or were set out after some months of such treatment into the open field.

Digitalis plants were found to require a cold dormant period in order to induce flower stalk formation. Miller (4) and Thompson (5) have reported a similar cold period requirement for the flowering of two other biennials, celery and cabbage.

Dried powdered leaf from young plants 4 to 6 months old has nearly double the glucoside content of that from older plants (9–17 months old) whether a flower stalk is formed on the older plants or not.

The authors desire to thank Dr. S. H. Culter and Mr. R. W. Henderson for preparing the U. S. P. tinctures, and Dr. Merl E. Fisk and Dr. Marvin R. Thompson for the assay results herein reported.

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STUDY OF GERMICIDAL AND ANTISEPTIC ACTIVITIES OF SOME DERIVATIVES OF 8-HYDROXY QUINOLINE.*

BY E. MONESS AND W. G. CHRISTIANSEN.

8-Hydroxy quinoline has bacteriostatic properties and is generally used in the form of its sulphate, which is water soluble. Matzumura (1) prepared 5-8-dihydroxy quinoline, and the presence of the additional hydroxyl suggested the possibility that such a compound may be soluble in an aqueous medium without resorting to salt formation.

This compound was prepared, as well as two chlorinated derivatives of it, and all were found to be soluble in a vehicle containing 30 parts of alcohol, 40 parts of

* Section on Practical Pharmacy and Dispensing, Madison meeting, 1933.

glycerin and 30 parts of water. Such a solution was found to be miscible with water in all proportions. In the germicidal and bacteriostatic tests 0.25% solutions of these compounds in alcohol-glycerin-water were used and diluted with suitable amounts of water at the time of test.

Chlorination of 5-8-dihydroxy quinoline always yielded a mixture of the mono-chlor and di-chlor compounds. Recrystallization from alcohol separated the mixture into two fractions: one was largely 7-chlor, 5-8-dihydroxy quinoline admixed with some non-chlorinated 5-8-dihydroxy quinoline, while the other was largely 6-7-dichlor, 5-8-dihydroxy quinoline, admixed with some of the mono-chlor derivative.

The germicidal and bacteriostatic activity of these compounds was found to be only moderate as seen from the following table:

Solution.	Dilution at Which Compound Kills. Typhoid. 5 Min.	Typhoid. 10 Min.	Staphylococcus. 5 Min.	Staphylococcus. 10 Min.	Dilution at Which Compound Is Bacteriostatic. Typhoid. 24 Hours.	Staphylococcus. 24 Hours.
5-8-dihydroxy quinoline	< 1–400	1–400	< 1–400	< 1–400	1–10,000	1–10,000
84.2% mono-chlor compound + 15.8% non-chlorinated dihydroxy quinoline	1–400	1–400	1–400	1–400	1–10,000	1–20,000
72.6% dichlor compound + 27.4% mono-chlor derivative	1–400	1–400	1–400	1–400	1–10,000	1–20,000

All the solutions are unstable due to the fact that the compounds oxidize easily; this is characteristic of compounds in which two hydroxyl groups are para- or ortho- to each other. Due to this oxidation the solutions darken with time from an original yellow-brown color to a dark red, and deposit a slight dark sediment.

According to Klarmann (2) the mono-ethers of hydroquinone exhibit germicidal power far greater than that of the original substance. It was thought that by preparing mono-ethers of 5-8-dihydroxy quinoline a similar increase in germicidal activity could be obtained, coupled with the additional advantage that such compounds would not be subject to oxidation and would give stable solutions. With this object in view, two compounds were prepared—the mono-ethyl and butyl ethers of 5-8-dihydroxy quinoline.

At first an attempt was made to fix the position of the alkoxy group by starting with 8-ethoxy quinoline, which was nitrated to 5-nitro-8-ethoxy quinoline and reduced to the amino derivative. This compound could be diazotized without any difficulty, but the attempt to replace the diazonium group by hydroxyl was unsuccessful; the yield was insignificant, and the reaction yielded complicated tarry and resinous compounds. Consequently the method of Klarmann was used, and the mono-ethers were prepared by the direct alkylation of 5-8-dihydroxy quinoline; the mono-ethers were separated from the di-alkylated derivatives by treatment

with alkali. When this method is used the exact position of the alkoxy group cannot be stated—it may be either in the 5- or 8-position.

When solutions of these compounds were made up in a vehicle consisting of a mixture of 30 parts of alcohol, 40 parts of glycerin and 30 parts of water, it was found that unlike the solutions of 5-8-dihydroxy quinoline, they were not miscible with water in all proportions. Thus a 1–400 solution of the mono-ethyl ether would become turbid on the addition of one volume of water, and would deposit crystalline material when two more volumes of water were added. A 1–400 solution of the mono-butyl ether deposited some crystalline material on being diluted with only one volume of water. However, both compounds formed water-soluble salts with great ease: the addition of one equivalent of tartaric acid to the alcohol-water-glycerin solutions to the ethoxy and butoxy compounds made it possible to dilute these solutions with water without having precipitation occur. The ethoxy compounds dissolve in aqueous tartaric acid; sufficient material was not available to enable us to make a similar test with the butoxy compound.

The germicidal and bacteriostatic activities were greatly enhanced, especially the germicidal activity of the butoxy compound.

Solution.	Dilution at Which Compound Kills.				Dilution at Which Compound Is Bacteriostatic.	
	Typhoid.		Staphylococcus.		Typhoid.	Staphylococcus.
	5 Min.	10 Min.	5 Min.	10 Min.	24 Hours.	24 hours.
Mono-ethoxy compound of 5-8-dihydroxy quinoline	1–400	1–400	1–800	1–800	1–200,000	1–400,000
Mono-butoxy compound of 5-8-dihydroxy quinoline	1–2000	1–2000	1–800	1–800	None	1–200,000

It is not quite clear why the bacteriostatic test for the butoxy compound was negative for typhoid bacilli, and this will be checked in the course of work now in progress on derivatives of hydroxy quinoline.

EXPERIMENTAL.

5-8-Dihydroxy Quinoline.—Ten Gm. of 5-nitroso-8-hydroxy quinoline was dissolved in a solution of 75 cc. of concentrated hydrochloric acid in 2700 cc. of water. The solution was kept at 95° C. and 16 Gm. of iron filings was added to it with constant stirring in small portions over a period of one hour. The solution was then stirred for one more hour at 95° C. It was filtered and evaporated to a volume of 150 cc. On cooling a crystalline mud separated out, which was filtered off. The dark brown crystalline substance was resuspended in 150 cc. of a mixture of equal parts of concentrated hydrochloric acid and water, brought to a boil and cooled. In this way 8 Gm. of light brown crystals of the hydrochloride of 5-8-dihydroxy quinoline was obtained. A sample dissolved in water and precipitated with sodium carbonate gives a grayish brown substance, melting point 180° C. The melting point for the purified substance as given in the literature is 181–183° C.

Chlorination of 5-8-Dihydroxy Quinoline.

5-8-Dihydroxyquinoline	4 Gm
Glacial acetic acid	80 cc.
Sulphuryl chloride	6 cc.

The compound was dissolved in the acid and to the solution was added slowly and with mechanical stirring a solution of the sulphuryl chloride in a little glacial acetic acid. A large excess of SO_2Cl_2 was used, since it was found that with a small excess the chlorination proceeded only partially.

An orange precipitate was obtained and was filtered off, dissolved in water and neutralized with sodium bicarbonate.

The filtrate was evaporated to a small volume and a second crop of orange crystals was obtained.

Yield—3.8 g. of a gray crystalline substance, m. p.—150° C.

Analysis.

Chlorine:	Found	21.22%
	Calculated for $C_9H_6O_2NCl$	18.30%
	Calculated for $C_9H_5O_2NCl_2$	30.88%

Evidently some of the di-chlor compound was also formed. By a fractional crystallization from alcohol we obtained two fractions, one analyzing as a mixture of 72.6% di-chlor and 27.4% mono-chlor compound, with a melting point of 163° C. and the other as a mixture of 84.2% mono-chlor compound and 15.8% non-chlorinated 5-8-dihydroxy quinoline, with a melting point of 128° C.

Both substances are easily soluble in alcohol and a solution in alcohol and glycerin is miscible with water in all proportions.

Preparation of the Mono-ethyl Ether of 5-8-Dihydroxy Quinoline.—4.03 Gm. of 5-8-dihydroxy quinoline and 3.9 Gm. ethyl iodide were dissolved in 4 cc. of alcohol. The solution was refluxed and a solution of 1.5 Gm. KOH in 4.2 cc. water was added dropwise during one hour; the refluxing was continued for 3 hours. A solution of 2 Gm. of KOH in a little water was then added, and on cooling the reaction mixture was extracted with ether. The ether extract was washed several times with a 10% solution of KOH; these alkaline extracts were combined with the alkaline reaction mixture and precipitated with acetic acid. A somewhat tarry precipitate was obtained which was purified by extracting with ether. This ether extract was washed with water, purified with charcoal, dried over anhydrous sodium sulphate and the ether was evaporated off; 0.8 Gm. of a yellowish crystalline substance was obtained, m. p. 96–98° C.

Analysis: Found—C, 69.7%; H, 5.37%; calculated for $C_{11}H_{11}O_2N$—C, 69.7%; H, 5.82%.

Preparation of the Mono-butyl Ether of 5-8-Dihydroxy Quinoline.—2.65 Gm. of 5-8-dihydroxy quinoline and 2.22 Gm. butyl bromide were dissolved in 2.65 cc. of alcohol. This solution was refluxed and a solution of 1 Gm. of potassium hydroxide in 3 cc. of water was added dropwise during an hour. The refluxing was continued for another 3 hours. The reaction mixture was worked up in the same manner as the ethoxy compound.

Yield—0.7 Gm. of yellowish white crystalline substance, slightly contaminated with a trace of an oily admixture; m. p. 92° C.

Analysis: Found—C, 70.60%; H, 6.50%; calculated for $C_{13}H_{15}O_2N$—C, 71.80%; 6.90%.

Both the ethoxy and the butoxy derivatives of 5-8-dihydroxy quinoline form orange, water-soluble salts, such as the hydrochloride and the tartrate.

The biological tests on compounds reported herein were made in the Biological Research Laboratories of E. R. Squibb and Sons and we gratefully acknowledge their assistance.

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A STUDY OF VEHICLES FOR MEDICINES.*

BY BERNARD FANTUS, H. A. DYNIEWICZ AND J. M. DYNIEWICZ.

V. COMPOUND ELIXIR OF CHLORAL AND BROMIDE.

As an "horrible example" of an undesirable N. F. preparation, must be mentioned the "Compound Mixture of Chloral and Potassium Bromide," which in addition to 20% each of chloral and bromide has 0.2% each of extracts of cannabis and of hyoscyamus added to it. The extracts are triturated with pumice and then the hot solution of the chloral and bromide is added, the mixture is set aside for twenty-four hours with occasional agitation, whereupon all but a trace of the extracts of cannabis and hyoscyamus is unceremoniously filtered out. Any statement as to the quantity of cannabis and hyoscyamus extracts contained in the finished preparation is a mere guess and worse. The quantity present is certainly not as given in the official dose statement; but a great deal less. In view of the unsatisfactory formula, it is not to be wondered at that it has a usage of only 0.25 per 10,000 prescriptions, according to the Gathercoal survey.

We must, therefore, either delete these insoluble ingredients or so modify the formula that they will remain in solution. With this in view we have experimented a great deal and would like to propose deleting the "Compound Mixture of Chloral and Potassium Bromide," which would be entirely justified by its limited use; and to introduce the following preparation to supersede the one deleted.

ELIXIR CHLORALIS ET BROMIDI COMPOSITUM.

Compound Elixir of Chloral and Bromide.

Synonym—Compound Mixture of Chloral and Potassium Bromide.

Chloral Hydrate	**62.5 Gm.**
Sodium Bromide	**125.0 Gm.**
Soluble Gluside	**0.5 Gm.**
Fluidextract of Cannabis	**12.5 cc.**
Fluidextract of Hyoscyamus	**25.0 cc.**
Alkaline Elixir of Eriodictyon (1), to make	**1000.0 cc.**

Mix the solid ingredients by trituration in a mortar and dissolve them in 900 cc. of alkaline elixir of eriodictyon. Add the fluidextracts of cannabis and of hyoscyamus and enough of the aromatic elixir of eriodictyon to make 1000 cc. Average dose: 4 cc. (1 teaspoonful).

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* From the Laboratory of Pharmacology of the College of Medicine of the University of Illinois.

Average dose contains:

Chloral Hydrate	0.25 Gm.
Sodium Bromide	0.50 Gm.
Fluidextract of Cannabis	0.05 cc.
Fluidextract of Hyoscyamus	0.10 cc.

The following reasons for the modification of the N. F. V formula may be advanced:

1. The new preparation contains the ingredients *in the relative proportion to their average dosage:* the proportions of the "mixture" (N. F. V) being entirely irrational even if all of the ingredients were retained:

PROPORTION OF ACTIVE INGREDIENTS.

	Dosage in "Mixture" of N. F. V per Teaspoonful.	Average U. S. P. Dosage.	Proposed Dosage per Teaspoonful.
Chloral	0.8 Gm.	0.5 Gm.	0.25 Gm.
Bromide	0.8 Gm.	1.0 Gm.	0.50 Gm.
Ext. Cannabis	0.008 Gm.	Fldext. 0.1 cc.	0.05 cc.
Ext. Hyoscyamus	0.008 Gm.	Fldext. 0.2 cc.	0.10 cc.

The proportions advocated in the new preparation should make it much more efficient, in view of the fact that we have here a synergistic mixture in which each of the ingredients, producing sedative and hypnotic action in a different way, should "potentize" each other, increasing the desired effect, while the undesirable effects are less than would be produced by a larger dose of each of the ingredients. It will be seen, for instance, that inasmuch as chloral is at least twice as powerful as the bromide the dose of the chloral and bromide are not in the proper relation in the old formula. The same thing is true of the relation of cannabis and hyoscyamus dosage. Furthermore, the dose of these two in the old formula is ridiculously small, even if all of it were retained.

2. *All the active ingredients are retained* in the new formula: there being no filtration. To be able to do this we have introduced an elixir of high (approximately 50%) alcohol content to improve the solvent qualities of the vehicle.

3. *To make the preparation as palatable as possible,* we have introduced the alkaline elixir of eriodictyon and added soluble gluside in the proportion of 1 to 2000.

4. *The title "Elixir"* is proposed for the new preparation, because being sweet and alcoholic this title appropriately classifies it. Furthermore, as has been shown by the Gathercoal survey, a Compound Elixir of Chloral and Bromide has much more extensive use than the Mixture.

5. *The "average dose"* proposed for the new preparation contains one-half of the U. S. P. average dose of each of the ingredients. "Bürgi's rule," which postulates that, "a mixture of substances each of which produces the same effect in a different way increases the potency of each of its ingredients," justifies one to believe that the proposed preparation, in teaspoonful doses, would have a greater sedative effect than half of the average dose of each of its ingredients. Hence, a teaspoonful should be an effective dose. If it is desired to give a full average dose of each of the ingredients, all that is necessary is to administer two teaspoonfuls of the new preparation which will, no doubt, act more powerfully than if each of the ingredients were given alone.

CONCLUSIONS.

1. It is proposed that the Compound Mixture of Chloral and Potassium Bromide be deleted from the National Formulary.

2. That a Compound Elixir of Chloral and Bromide be introduced in its stead.

3. This elixir to contain the active ingredients in the relative proportion of their average U. S. P. dosage.

4. The preparation to be stabilized and made palatable by means of the alkaline elixir of eriodictyon.

THE PROTECTION OF PRESCRIPTION LABELS WITH LACQUER.*

BY WILLIAM J. HUSA[1] AND LYDIA M. HUSA.

Considering the dangers involved when mistakes are made in the use of medicines, it is of the utmost importance that pharmacists take proper precautions to insure the legibility of labels on prescriptions and to make sure that the patient understands the directions. With the wide-spread use of the typewriter at the prescription counter, the difficulties arising from poor penmanship are disappearing. Pharmacists who do not have typewriters available should take care to write legibly, using pens which are in good condition; it would also be advantageous to use a better grade of ink, such as India ink, which is so much more permanent than ordinary writing fluids.

The better type of pharmacist pays particular attention to the labeling and other points in the finishing of the prescription and he may sum up his activities by saying that every prescription must be "right" when it leaves the store. If a well-typed, properly affixed label becomes smeared and illegible through handling by the patient, the pharmacist is apt to feel that this is the responsibility of the patient. He may say that the patient should be careful not to spill the medicine on the label, that handling with wet or soiled hands should be avoided, and finally that if the label shows signs of becoming illegible, it should be returned to the pharmacist for relabeling. All this may be true, yet any pharmacist who critically examines his own home medicine chest will admit that the gradual loss in legibility of labels is a real menace. The bad condition of many of the labels on prescriptions brought back for refilling is frequently a troublesome factor at the prescription counter.

From these considerations it is evident that the adoption of a practical method for increasing the permanency of prescription labels would bring about a worthwhile improvement in pharmaceutical service. The use of a label varnish naturally suggests itself and the older pharmaceutical journals often gave formulas for label varnishes, which, however, for one reason and another, have never come into general use by pharmacists.

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[1] Head Professor of Pharmacy, University of Florida.

NOTE: See abstract of discussion in minutes of Section on Practical Pharmacy and Dispensing.

During the past fifteen years, with the development of a new type of nitrocellulose giving solutions of low viscosity, and the introduction of synthetic resins and new solvents, great strides have been made in the manufacture and use of lacquers in the finishing of automobiles, furniture, etc. The use of clear lacquer (containing no pigment) has come into use for protecting the bindings of books and similarly lacquer is used for increasing the permanency of shipping labels, etc.

For the lacquering of labels, a quick-drying, colorless or light-colored lacquer is preferable. Commercial label varnishes are now available which are advertised as being quick-drying, acid proof, alkali proof, oil proof, alcohol proof and washable. These have been recommended for use in chemical stock rooms, research laboratories and museums.

Since it appeared that the use of a suitable lacquer on prescription labels would be advantageous, we have made some tests along this line, using one of the commercial label lacquers. It was observed that the lacquer penetrated the labels too much, making them somewhat translucent, particularly at first. It was thought that this could be corrected by first applying a coat of U. S. P. collodion. Comparative tests were carried out, using coatings as follows on the labels of prescription bottles:

No. 1. Lacquer.
No. 2. Collodion + lacquer.
No. 3. Lacquer + lacquer.
No. 4. Collodion + lacquer + lacquer.
No. 5. Plain label (for comparison).

The coatings were applied with a half-inch lacquer brush. Where successive coatings were used, they were applied five minutes apart.

Examination of the labels showed that the use of an undercoat of U. S. P. collodion was advantageous, as it dried rapidly and largely prevented penetration of the lacquer, which thus remained to a greater extent on the surface where it is needed. In case of No. 3 (two coats of lacquer), the drying appeared to be slow and this was further evidenced by the fact that the labels on two such bottles adhered when put away together after standing about half an hour after the coatings were applied.

As a test of efficiency, aromatic fluidextract of cascara sagrada was smeared on the labels. The plain label was badly stained, of course, and could not be washed without damage. The label having one coat of lacquer (No. 1) stained slightly and showed slight staining after washing with water; also it was evident that one coat gave insufficient protection against water. In case of No. 2 (collodion + lacquer) the fluidextract did not stain the label, which could easily be washed perfectly clean; this was also true of No. 3 (two coats of lacquer).

From the results of our tests, the following recommendations are made:

1. For prescription labels: a coat of U. S. P. collodion followed by a coat of label lacquer.
2. For stock bottles, bottles used in hospital wards, etc.: a coat of U. S. P. collodion followed by two coats of label lacquer.

The above recommendations are made on the basis that an extra coat of lacquer is desirable for bottles subjected to particularly hard or frequent usage, as in hospital wards.

The protection of labels as described, making them washable and durable, is not a frill which can just as well be omitted, but represents, rather, a technique which should be used in every retail and hospital pharmacy. In the hospital pharmacy, much time will be saved, since it will not be necessary to replace labels so frequently. The permanence and greatly extended period of legibility of such labels will prevent accidents and save lives. We need only recall the recent tragedy in an Australian hospital, where the life of a patient was lost because a young nurse administered belladonna instead of syrup of figs. The report of the case (1) states that "both were ordinary white glass bottles, and the labels were stained and almost illegible."

There is no reason why pharmacists should not take pride in sending out prescriptions with labels which are not only legible when they leave the store, but which are so durable and washable that they will remain legible a long time afterward.

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A STUDY OF AROMATIC ELIXIR.*

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An elixir, similar in formula to the present official aromatic elixir was made official in the U. S. Pharmacopœia VI, with the title, Elixir Aurantii. The synonym was Simple Elixir. It was made by percolating cotton, which had been soaked with oil of orange. The menstruum used was composed of water 3 parts and alcohol 1 part.

In the U. S. Pharmacopœia VII, this elixir was replaced by Elixir Aromaticum, and the formula considerably modified. Compound spirit of orange took the place of oil of orange of the previous formula and cotton as a filtering agent was replaced by precipitated calcium phosphate. The only change in the formula in the U. S. Pharmacopœia VIII was that purified talc replaced the precipitated calcium phosphate. Aromatic Elixir, in title, formula and process of making, has remained unchanged through the revisions of the Pharmacopœia since the Eighth.

This fact should not be taken to mean that the formula is, in all respects, wholly satisfactory. A review of the literature reveals that an endless number of complaints have been made about it, mainly, because it consumes so much time in filtering, while others are, that it is too sweet and its alcoholic content too high for certain uses as a vehicle.

Like many of the workers who have preceded us in the study of this preparation, we have sought to acquaint ourselves with the problem, with the hopes of being able to suggest an improved formula. To this end our study presents a review of the literature, under the following headings:

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1. **Flavoring Substances.**
2. **Alcohol and Sugar Content.**
3. **Clarifying Agents and Methods of Making.**

A summary of our studies and recommendations is also given.

THE FLAVORING AGENTS USED IN AROMATIC ELIXIR.

In 1871 (1) the Newark Pharmaceutical Association proposed the following formula for aromatic elixir:

Cort. Aurantii	4 drachms
Sem. Coriand.	2 drachms
Sem. Angelicæ	2½ drachms
Cocii Cacti	1 drachm
Spt. Vini Deod.	12 ounces
Aquæ	10 ounces
Glycerinæ	5 ounces
Syrupi	5 ounces

Directions were given to percolate 2 pints. This, it was stated, "is a pleasant vehicle for administering nauseous remedies." In the 1871 Report of the Committee on Unofficial Formulas of the AMERICAN PHARMACEUTICAL ASSOCIATION (2) a formula for simple elixir was recommended in which oils of anise, caraway, cinnamon and fennel were the chief sources of flavor. In 1872 Eberback (3) percolated fresh orange peel, powdered star anise, and cardamon with equal parts of alcohol and water. To this percolate syrup, caramel and the proper amount of water were added. Hancock (4), in 1873, reported that a most satisfactory simple elixir could be made from spirit of orange. Markoe, at the same time, expressed a preference for the tincture made from the fresh orange peel. Later, Hancock (5) proposed a formula which contained spirit of orange and cinnamon water as the flavoring agents. About the same time Remington (6) objected to the use of oils for making the elixir and suggested a formula composed of orange water, cologne spirit and syrup, with Spiritus Vini Gallici as optional for the preparation.

In 1875 the Committee on Formulas for Elixirs of the AMERICAN PHARMACEUTICAL ASSOCIATION (7), reported a formula for simple elixir that contained spirits of orange and cinnamon. Maddox (8), in 1880, suggested the use of oils of lemon, cassia and caraway, in a simple elixir which he considered superior to any he had used.

The United States Pharmacopœia VI contained a formula for Elixir Aurantii (simple elixir) with oil of orange as the only flavor. "The New York and Brooklyn Formulary of Unofficial Preparations" (11) proposed a formula for Aromatic Elixir, in which Aromatic Spirit was the flavoring agent. Aromatic spirit was an alcoholic solution of the extractive principles of fresh orange and lemon peel, bruised coriander and oil of star anise. The same formula, together with four others, was proposed in "A Preliminary Draft of a National Formulary" (12). The second of these formulas was composed of solutions of the oils of orange, cinnamon, anise, bitter almond and tincture of cardamon. The third contained only oil of orange and orange flower water. The fourth contained the tinctures of fresh orange and lemon peel and orange flower water. The fifth was made by percolating cinnamon, nutmeg, cassia, cloves, myrrh and aloe with the addition of a small amount of orange flower water.

Elixir Aromaticum U. S. Pharmacopœia VII contained compound spirit of orange as the flavoring agent. In 1896, Ott (14) suggested that the elixir should be made from the oils rather than from the compound spirit of orange. McIntyre pointed out that the use of the compound spirit of orange was a means of assuring greater accuracy in measuring small quantities of the oils and that the spirit would keep better than the oils, so far as flavor was concerned. In 1902, Bradford (16) suggested the use of tincture of sweet orange. Scoville (19), two years later, proposed a formula, which, he said, corresponded to the official product in character and strength but was an improvement in vigor and delicacy. He suggested the use of the tinctures of fresh orange and lemon peel, oil of coriander and white wine. Johnson (25), however, after considerable experimentation, decided that the official formula containing compound spirit of orange could hardly be improved upon as a flavor. In 1912, Egan (29) said that the aroma and flavor of the

official elixir could be greatly improved by dissolving the compound spirit of orange in the alcohol and allowing the solution to remain in a refrigerator for 48 hours. The *Druggists Circular* (34) printed a formula in which soluble orange was used. The editor pointed out, however, that such flavors were looked upon with suspicion. Beringer (39) suggested the addition of 20 cc. of oil of cinnamon to each liter of the compound spirit of orange for this elixir. Jones (41) suggested the use of terpeneless oils of orange and lemon together with anethol and oil of coriander in a concentrated soluble formula, 30 cc. of which, when properly diluted with alcohol, syrup and water, made a good simple elixir.

THE ALCOHOL AND SUGAR CONTENT OF AROMATIC ELIXIR.

Aromatic elixir seems to have been used as a vehicle for a number of years before there wss much question as to its sugar and alcohol content. In 1902, Bradford (16) suggested an improved formula in which glycerin represented 25% of the total volume and contained neither sugar nor syrup. Fleet (20) later proposed a similar formula which he termed, Elixir Aurantii Sine Saccharum. Heffner (22), in 1906, suggested that care should be exercised in using the official elixir as a vehicle in children's medicines because of its high alcoholic content and because of its incompatibility with certain salts. Johnson (25) also considered the alcohol content too high and after some study of the problem recommended a formula containing about 6.5% by volume of alcohol. Fantus (38) suggested that the alcohol content of this preparation should be adjustable to any desired strength. He proposed a formula containing 5% alcohol, capable of further fortification with alcohol as occasions required. Egan (40) proposed a formula containing about 8% alcohol and approximately 35% by volume of glycerin. He gave, as his reasons for these changes, the prohibition regulations and the scarcity of sugar. He claimed that his formula made a product not only equal in quality to that of the official preparation, but that it was cheaper.

In 1923, Snow and Fantus (42) found objection to the high alcohol content of simple elixir and proposed a formula for an aqueous elixir which contained 5% of alcohol and 20% by volume of glycerin, the latter replacing the alcohol of the official formula. They maintained, also, that their formula was a better solvent for salts that are often prescribed. The *Druggists Circular* (43), in commenting upon non-alcoholic formulas for simple elixir, said that without alcohol it would be lacking one of its principal ingredients. A formula suitable for diabetics was proposed by Snow and Fantus (45) in 1930. It contained gluside 20 Gm., glycerin 200 cc., alcohol 250 cc. and water enough for 1000 cc. This formula, it is suggested, is miscible in all proportions with alcohol and water. The alcohol content may be reduced by diluting it, in which case it would serve as a vehicle for the bromides.

CLARIFYING AGENTS AND METHODS OF MAKING AROMATIC ELIXIR.

The most vexatious problem connected with the manufacture of simple elixir is that of clarification. Elixir Aromaticum is widely used as a vehicle, and it is generally acceptable, but there is almost universal complaint as to the time consumed in filtering it. For this reason many workers have suggested numerous ways of speeding up the filtration time for this preparation. To accomplish this without seriously modifying the formula has proved to be no easy task.

In 1873, Hancock (5) used paper pulp as the clarifying agent, saying that it was free from the chemical objections of magnesium carbonate and chalk. Even though the finished elixir was turbid, it could be used for some purposes. In 1880, Maddox (8) used magnesium carbonate to clarify what he called a superior formula. Moore (9) also recommended the use of magnesium carbonate. Simple elixir, U. S. Pharmacopœia VI was made by pouring a solution of alcohol, 1 part, and water, 3 parts, over cotton packed in a percolator which had been wetted with oil of orange. The sugar was dissolved in the percolate and the product strained. "The New York and Brooklyn Formulary of Unofficial Preparations" (11) contained a simple elixir formula which was clarified with phosphate of calcium. In "A Preliminary Draft of a National Formulary" (12) five simple elixir formulas were proposed. For one of these, calcium phosphate was the clarifying agent, for another, carbonate of magnesia and for two others, talcum. Elixir Aromaticum, U. S. Pharmacopœia VII was clarified by the use of calcium phosphate. In 1896, Ott (14) used precipitated calcium phosphate in a proposed elixir formula. Talcum appeared in the

formula for Elixir Aromaticum U. S. Pharmacopœia VIII, replacing calcium phosphate in the formula of the previous issue. Parry (15) suggested a formula which, he said, needed no clarifying agent if allowed to stand two weeks before filtering. Dunning (17) saved time in making this elixir by adding the calcium phosphate to the mixture of compound spirit of orange, alcohol and water, in which, after filtering, sugar was dissolved. This avoided the tediousness of filtering a thick syrupy solution. Caldwell (18), in 1903, reported that the preparation could be made to filter clear at once, if mixed in the proper manner. Fleet (20) advised sprinkling the filter paper with calcium phosphate, before filtering, rather than mixing it with the liquids as is usually done. According to Toplis (21), simple elixir is, "one of the greatest time consumers of the U. S. P." He modified the official process by mixing the compound spirit of orange with the talcum. To this was added the solution of alcohol and water, which was filtered after the manner of making official waters. The required amount of sugar was dissolved in this filtrate. Posey (23) speeded the time of making even more by mixing the talc, the compound spirit of orange and the water and then filtering. The syrup and alcohol were then added to the filtrate. Doyle (24), in 1909, used magnesium carbonate as the clarifying agent. The mixture was allowed to stand until a clear supernatant liquid separated which, it is stated, filtered clear in a short time.

In 1910, the *Western Druggist* (27) printed a formula in which it was suggested that the alcohol be added in part to the compound spirit of orange, talc and water and the mixture filtered. The remainder of the alcohol was added to the syrup, which in turn was dissolved in the clear filtrate. Dunn (28), under the title of "Shortcuts and Improvements," suggested that the compound spirit of orange and alcohol be mixed with kaolin and filtered, and that water be added to this filtrate, in which sugar was then dissolved, and the whole filtered through cotton. Five grams of magnesium carbonate, according to Sass (30), gave better results in filtering than did the required amount of talcum. In 1913, Daniel (31) modified the official process for simple elixir somewhat, but said, "It is my opinion that quick and easy, and first class work are incompatibilities." Possehl (32), in 1914, suggested that the official elixir could be improved by first making a water, in the usual way, from the compound spirit of orange and talc, and adding to it the syrup and alcohol. Fried (33), in 1914, said, "one of the easiest preparations to make is aromatic elixir providing a few changes in procedure are made." He suggested that the syrup should be replaced by sugar and added after filtration and then the whole strained, if necessary. Satz (35) filtered the aqueous-compound spirit of orange mixture with talc and to this added the syrup and alcohol. Scher varied this a little. He filtered the compound spirit of orange, alcohol and water mixture with talc and added the syrup to the filtrate. Burge (36) followed Scher's procedure, but used paper pulp as the clarifying medium. Concerning aromatic elixir, Cook (37) said, "It is unfortunate that the purified talc, which is not a satisfactory filtering medium, was not replaced by purified siliceous earth (Kieselguhr), which has been made official." Purified siliceous earth not only speeds the rate of filtering but clarifies the elixir promptly. Egan (40) maintained that the use of purified siliceous earth, as compared to talc, resulted in clearer elixirs. Jones (41) spoke out of much experience with simple elixir when he said, "Its clarification is very trying on one's patience, and the usual result is a cloudy preparation, even after many repeated filtrations." After a study of the effect of various clarifying agents upon "The Hydrogen-Ion Concentration of Aromatic Elixir," Krantz and Carr (44) concluded that normal magnesium carbonate is admirably suited for use as a filtering agent in this preparation, because it filtered rapidly and yielded an almost neutral elixir. In 1930, Shiflett (46) offered a modified procedure quite similar to one reported in 1910 (27). A solution of 150 cc. of alcohol and 300 cc. of water is made. The compound spirit of orange is then triturated with the talc and mixed with 350 cc. of the above alcohol-water solution. After filtering, 375 cc. of syrup are added to the filtrate. To this is added the remaining 100 cc. of alcohol, and then water enough for 1000 cc. It is claimed that this process requires but one-tenth the time of the official procedure. "If there is any discrimination in flavor, it is in favor of this non-official process." Silver (47) found fault with Shiflett's procedure and offered a slightly different one. Burlage (48), in 1932, studied five methods for making simple elixir: 1. The U. S. P. method modified as to the order of mixing; 2. The U. S. P. procedure unmodified; 3. Shiflett's Method; 4. Silver's Method; and 5. The U. S. P. Method, modified by using double the specified amount of talc. As to speed of filtration, he rated the methods of Shiflett and Silver about equal and superior to the present official and proposed modifications.

Fantus, Dyniewicz and Dyniewicz (49), in 1933, criticized several methods and formulas, which have been proposed. They formulated the three following rules for preparing the elixir: 1. The viscosity must be kept low until after clarification. 2. Filtration through talc and other absorbents must be abandoned, because it consumes time and wastes oil. 3. One must avoid precipitating the oil globules so fine that they will pass through a filter paper and, in turn, a longer time for saturation should be allowed. They propose making the elixir by mixing all of the water with the alcohol, adding the compound spirit of orange, and allowing it to stand for 24 hours, being frequently agitated, then filtering through a hard filter, without the use of any absorbent. Lastly dissolve the sugar in the filtrate.

EXPERIMENTAL PART.

In the face of the rather discouraging results of many workers, to speed up the time of filtration of Elixir Aromaticum without the loss of its very acceptable aroma and flavor, we attempted the impossible. It was decided at the outset that the time consumed in filtering the official simple elixir is an item of no mean consideration. Furthermore, it was assumed that it would be rational to sacrifice, if necessary, a part of the flavoring qualities of the present formula, for one slightly less pleasing, if the objections to the present process could be removed. We have tried, in the work we have done, to incorporate the suggestions of other investigations, although not always in agreement with them upon every point.

In an attempt to speed up the process for making aromatic elixir, a series of 14 elixirs were prepared. The U. S. P. X formula and procedure were used as a basis for the several modified formulas. All deviations from the official formula and procedure are noted for each modification. 1000-cc. quantities were prepared in most cases.

THE MODIFICATIONS.

1. Elixir Aromaticum, U. S. P. X. The formula and procedure of the Pharmacopœia were used and followed and are not repeated here.

2. Paper pulp was substituted for purified talc.

3. Washed talc was substituted for the official talc. This was prepared by washing the talc repeatedly with water by decantation for the purpose of removing all of the very fine filterable particles.

4. The compound spirit of orange was mixed with the talc, to this was added, in portions, the syrup, alcohol and water previously mixed. This was allowed to stand 24 hours and filtered in the usual way.

5. Water and sugar were substituted for the syrup.

The compound spirit of orange was dissolved in the alcohol, and water added in portions to make 818 cc. This was mixed with the talc and filtered. The sugar was dissolved in this filtrate and made up to 1000 cc. by the addition of a solution of alcohol 1 and water 3. (This is the method of Toplis *q.v.* (21).)

6. After the method of Scher, *q.v.* (35) the compound spirit of orange, alcohol and water were mixed with the talc and filtered as usual. The syrup was added to the clear filtrate and the quantity made up to 1000 cc. according to the official method.

7. Glycerin, 125 cc., was substituted for an equivalent amount of syrup. The compound spirit of orange, alcohol, water and talc were mixed and filtered, as officially directed. The syrup and glycerin were added to the clear filtrate and the volume made up to 1000 cc. as usual.

8. An elixir was made by saturating the solvents. The alcohol, syrup and water were carefully mixed. Compound spirit of orange was then added dropwise, with shaking after each addition, until the solution became saturated.

9. Number eight was repeated with a slight change in the solvent. 125 cc. of glycerin were used to replace an equivalent amount of syrup. The alcohol, glycerin, syrup and water were then mixed. Compound spirit of orange was then added as in number eight.

10. An elixir was prepared according to the Shiflett formula (46). Dilute 150 cc. alcohol and 300 cc. of distilled water. 350 cc. of this solution were mixed with the mixture of talc and compound spirit of orange, and the whole filtered. The filter was finally washed with the remaining 100 cc. of alcohol and water solution. Syrup was then added to this filtrate, in divided portions with agitation after each addition. The remaining 100 cc. of alcohol was then added and the volume made up with water, if the amount needed was small; with alcohol 1 part and water 3 parts, if the amount needed was large.

11. Sugar and water were substituted for syrup. The compound spirit of orange and talc were mixed. 575 cc. of water were added to this mixture and the whole agitated frequently for 15 minutes and then filtered in the usual way. In 550 cc. of the clear filtrate, 320 Gm. of sugar were dissolved, 250 cc. of alcohol then added and the volume made up to 1000 cc. by addition of the first clear filtrate.

12. The U. S. P. simple elixir was prepared, using purified siliceous earth instead of the talc.

13. The U. S. P. simple elixir was prepared, using kaolin instead of the talc.

14. The U. S. P. simple elixir was prepared using magnesium carbonate instead of the talc.

TABLE I.

Formula No.[1]	Appearance of Finished Product. Clear.	Cloudy.	Colored.	Times Filtrate Was Returned Before It Cleared.[2]	Rank as to Time Required to Prepare.[3]	Condition after Two Years.[4] Odor.	Taste.	Sediment.
1	cl	...	...	7	13	g	g	s
2	cl	f	...	22	14	g	g	s
3	cl	...	...	4	11	g	g	s
4	cl	...	...	5	12	g	g	s
5	2 w	1st	...	4	10	g	g	pro
6	2 w	1st	...	4	8	g	g	s
7	2 w	1st	...	4	9	g	g	pro
8	...	clo	...	nf	5	p	p	oil
9	...	clo	...	nf	6	p	p	oil
10	2 d	1st	...	3	7	t	t	s
11	cl	...	...	3	3	g	g	s
12	cl	...	...	1	4	g	g	...
13	cl	...	...	2	2	g	g	...
14	cl	...	sy	0	1	g	g	...

ABBREVIATIONS: cl, clear; 2 w, after 2 weeks; 2 d, after 2 days; f, faintly; 1st, at first; clo, cloudy; sy, slightly yellow; nf, not filtered; g, good; p, poor; t, terebinthinate; s, slight; pro, pronounced; oil, oil on surface.

[1] See preceding pages for formulas and methods of making.

[2] Approximately 100-cc. portions were returned each time.

[3] Number one required the shortest time, about an hour, and the longest time, about 24 hours. [4] Two years' time applies to Nos. 1 to 11; about two months only to Nos. 12, 13 and 14.

Table I gives, in brief, our observations of the fourteen modifications of the simple elixir made as outlined above. They were observed (1) with respect to clearness and color, (2) the number of times that it was necessary to return 100-cc. portions back through the filter before the filtrate became clear; (3) a comparative scale of the speed or time required to complete each product, and (4) condition as to odor, taste and sediment after standing in storage for two years.

The results, as expressed in Table I, verify many of the observations of other workers upon this problem, as for instance the difference in filtering time with talc as compared to purified siliceous earth or magnesium carbonate.

A SIMPLE ELIXIR OF LOW ALCOHOL CONTENT.

We are cognizant of the objections that have been made to making a simple elixir by the so-called "aromatic water" method and also that it has been said that aromatic elixir with little or no alcohol in it is without one of its very important constituents. Even so we chose to experiment with formula Number 11 which has been given. Three lots were made by the "aromatic water" process. These were termed Lots A, B and C and each contained successively smaller percentages of alcohol. Lot A contained 15% alcohol; Lot B, 10% and Lot C, 5%. These three lots kept perfectly for more than six weeks. The only difference in taste that we could detect, was attributed by us to the alcoholic content. We therefore concluded that a reasonably good aromatic elixir, with any desired alcohol strength, is possible.

SIMPLE ELIXIRS AS OTHER ELIXIR VEHICLES.

A. Elixir Glycyrrhizæ U. S. P. X.—Since Elixir Glycyrrhizæ is a preparation composed chiefly of aromatic elixir, five lots of it were prepared using the modified formulas numbered 1, 11, 12, 13 and 14, previously described. These five lots were observed over a period of several weeks. They were, from all appearances, quite alike, even in the slight sedimentation that resulted.

B. Elixir Potassii Bromidi N. F. V.—Approximately 30% Aromatic Elixir is contained in this preparation. Three lots of it were prepared, using elixir modification formulas, numbering 1, 11, and a modification of number 11 containing but 10% alcohol described as Lot B in the paragraph under "A Simple Elixir of Low Alcoholic Content."

These three preparations were made according to the official directions. They were studied over a period of several weeks. No observable differences between them were noted during this time.

These observations, though few in number, do indicate that some of the modified simple elixirs, which have been described, are usable and seem to compare well in that respect with the official elixir which is tedious to prepare and of questionable alcoholic content.

A PROPOSED SIMPLE ELIXIR FORMULA.

As a result of our study of the official simple elixir, especially with respect to

the difficulties of making, as well as to other objections that have been made, the following formula and method are suggested for the preparation of aromatic elixir:

Compound spirit of orange	12 cc.
Purified talc	30 Gm.
Sugar	320 Gm.
Alcohol	The desired amount
Distilled water, to make	1000 cc.

Carefully mix the compound spirit of orange and talc by trituration. Add about 800 cc. of water, in convenient portions, and triturate after each addition. Agitate frequently for about 15 minutes and filter in the usual manner. Dissolve the sugar in 550 cc. of the clear filtrate and to it add the amount of alcohol desired. Finally make up to 1000 cc. with the required amount of the clear filtrate.

CONCLUSIONS.

Although this recommended formula may contain somewhat less of the flavoring principles than does the official elixir, we think it is sufficiently strong in flavor to serve as a good vehicle. We recommend it for the following reasons:

1. The time required to prepare it is approximately one-tenth that necessary for the present official simple elixir.

2. The alcohol strength of this elixir may be varied at will without modifying the technique of making.

3. The preparation is always the same clear product regardless of a variation in the alcoholic content.

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C. LEWIS DIEHL.*

BY JOHN E. KRAMER.

The name Diehl is synonymous with pharmacy, pioneer and progress. C. Lewis Diehl's connection with the first is well known to every one acquainted with the history of American pharmacy. This profession was evidently his very life and being, as attested to by his career.

That he was a pioneer can be seen in a cross section of his advancement through life. Less than fifty years after the Philadelphia College of Pharmacy had been founded in 1821, Mr. Diehl was the founder of the Louisville College of Pharmacy in Louisville, Ky., and was elected and reëlected, successively, president of that institution for eleven years. He proved to be a pioneer as one of the members of the first Board of Pharmacy of Kentucky, retaining that post for twelve years. He opened two drug stores in Louisville, and was one of the pioneers in research work along pharmaceutical lines, being noted for his work on percolation, along with Procter, Squibb and others of his time. Incidentally, this process of extracting the principals of drugs by percolation, developed in America, remained a typical American process, as the European countries never became enthusiastic over the idea, and almost totally ignored it.

Pharmacy, in the time of Diehl, was in an early stage of organization in the south and southwest, and also in the matter of research and the establishing of American pharmaceutical customs. Prof. Diehl was indeed a leader of the pioneers in these fields.

The third synonym is progress. Something once started must be continued, to make it worth while. Professor Diehl applied this idea to pharmacy, for, after

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establishing the College and the State Board, he continued to serve with them, in some capacity, until his death. His connections with the local and national pharmaceutical associations were not stationary, but progressive. As the Reporter on the Progress of Pharmacy for the AMERICAN PHARMACEUTICAL ASSOCIATION, Diehl's reports were pieces of masterful, scientific work. In the year in which he was president of this organization, 1874, his report filled 278 printed pages and comprised the greater bulk of the YEAR BOOK. Reports of this great length and scope were customary to the man. As one member stated, his reports alone were worth the yearly dues.

Professor Diehl was also associated with the revision committees of the United States Pharmacopœia and the National Formulary, doing his greatest work with the N. F. committee as chairman of that body. His connections with both these books of pharmaceutical standards helped in the great work of revision by preventing duplication of formulas and contents. Again progress was his watchword.

A short sketch of Prof. Diehl's life shows his continued work for pharmacy. He was born in 1840 in Bavaria, and at the age of eleven came to America, immediately entering a school near St. Louis. Three years later he left the school and came to Philadelphia to be with his father. His first job was with a perfumer and drug sundryman, but soon after became apprenticed to a pharmacist-physician. While serving his apprenticeship he attended the Philadelphia College of Pharmacy and graduated in 1862. After service in another drug store he entered the employ of John Wyeth and Brother.

The Civil War then became the foremost topic and action of the day and Diehl answered the call to arms, serving in the 15th Pennsylvania Regiment until he was severely wounded at the battle of Stone River, from which wound he never fully recovered. Until the close of the war he served the Government as a chemist, and then went to Louisville to become manager of the Louisville Chemical Works.

It was in that city that he did his pioneer work of establishing his stores, the College and the State Board, and served as president of the Kentucky Pharmaceutical Association. From there, too, he conducted all his activities with the various committees of national scope; and in that city he died, in 1917.

Professor Diehl was a constant contributor to journals and conducted many scientific researches. His reports were masterpieces of science, well balanced and constructive. In recognition of his work he received the honorary degree of Master of Pharmacy from the Philadelphia College of Pharmacy and Science, in 1887.

Friendship and respect he won; his passing brought forth many sincere expressions of sorrow from men of foremost importance in all walks of life. There was not so much of the romance about Professor Diehl as with others of his and earlier times. Simplicity and earnestness marked his endeavors for pharmacy and his only ambition was the furtherance of his beloved profession.

REFERENCES.

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THE DEPARTMENT OF THE AMERICAN ASSOCIATION OF COLLEGES OF PHARMACY

C. B. JORDAN—CHAIRMAN OF EXECUTIVE COMMITTEE, A. A. C. P., EDITOR OF THIS DEPARTMENT.

Editor's Note: Do colleges of pharmacy give sufficient work in pharmacology? I believe I agree with Dean Serles that they do not and that, with the extension of the course to four years, this should be corrected. However, the cost of a laboratory course in pharmacology to a large group of students may be expensive unless great care is taken to keep the expenses down. Demonstration by the instructor of the pharmacological reactions that "run into money" will be helpful, but a course that consists entirely of such demonstrations will not suffice. Dean Serles has presented a sane view of the problem and has given suggestions that will be helpful to any college contemplating such a course.—C. B. JORDAN, *Editor.*

OUR FOUR YEARS' EXPERIENCE WITH THE TEACHING OF PHARMACOLOGY AT SOUTH DAKOTA STATE COLLEGE.

BY E. R. SERLES.*

The advent of the four-year course as a minimum requirement for graduation from member colleges of this association has brought forth a divergence of opinion as to what subject material, new or old, should properly receive further development. The Syllabus published in the latter part of 1932 has projected an outline of the old and some new courses, which although not obligatory, will undoubtedly influence many of the schools and colleges in reshaping their curricula. Perhaps the most radical departure from the old order advocated by the Syllabus Committee was the dropping of the term Materia Medica and the inclusion of the term Pharmacology in lieu thereof.

Pharmacology is not a new science. It is not new to Pharmacy for our leading pharmaceutical houses have been employing a knowledge of its fundamental principles in drug standardization for many years.

The teaching of this science in colleges of pharmacy is, however, new. A survey of our college catalogs of a few years ago fails to show more than one or two schools engaged in the teaching of any phase of pharmacology except posology and toxicology and in most cases such courses were wholly didactic.

Realizing the value of laboratory demonstration in the teaching of chemistry, pharmacy and dispensing, we of the faculty of State College conceived the idea that the teaching of dosage and related functions of drugs could be more easily accomplished if we could but show the effects of a single drug or a group of drugs upon living organisms.

Perusal of medical college catalogs and laboratory outlines of courses in pharmacology offered in such schools, together with experience gained in the chemical war service clearly indicated that a course in pharmacology for pharmacy students was feasible and, what was more important, desirable.

Pharmacology was accordingly offered as an advanced elective to those students who had completed courses in physiology, pharmacognosy, materia medica and chemistry. The ease with which they adjusted themselves to the complicated laboratory procedure of taking a blood pressure, giving anesthetics, hypodermic and

* South Dakota State College.

intravenous injections proved to us that here was a means of fixing the facts covering drug action and dosage long overlooked in our methods of teaching this important part of a pharmacist training.

Dr. M. R. Thompson in a paper before this group emphasized the adaptation of pharmacologic procedure to bioassays as being the phase of pharmacology which should receive our attention when trying to build a course for pharmacy students. This may be true, but it has been my experience, and particularly so as a member of the U. S. P. Bio-assay Committee, that this part of the work is highly specialized, and requires the best of apparatus, controlled conditions and a profound knowledge of the fundamentals of pharmacology, if more than just the technique of the experiment is to be demonstrated.

Again we must keep in mind that if we are to drop the subject hitherto known as Materia Medica, and put in its place Pharmacology, we must provide some means of conveying to the student a knowledge of that vast wealth of information concerning the origin, composition and properties of remedial agents. Such information, I believe, should be included in the courses of pharmacognosy, if the material is of a crude drug nature and in the courses of pharmacy if the substance be a chemical.

For the past four years we have been shaping our courses with this end in view: Pioneering in this field we have made mistakes, but most of them have been on the side of omission rather than commission.

First, we found our students lacking in a knowledge of physiology and comparative anatomy, especially of the smaller animals used in experimental work. *Second*, the ability to interpret physical phenomena, such as rate of injection, kinds of material injected and site of injection were problems for both the operator and student to master. *Third*, organization of laboratory experiments, so that the cost of operation is not too great is necessary for one must recognize that pharmacology properly taught is expensive. The source and care of laboratory animals is the chief factor in determining the cost of the course once the laboratory is equipped.

The course as it has been given has been chiefly for advanced students, where the numbers were few, consisting of two lectures per week and two three-hour laboratory periods. I should like to emphasize the fact that the laboratory periods should be at least three hours in length and could well be extended to a full half day for the more extensive animal experiments.

Our new course designed to include the students who are to receive a general training for the practice of retail pharmacy will consist of three lectures per week on the theory of drug action and a single laboratory period, chiefly demonstration.

In this connection I assume that you will be most interested in the laboratory procedures. For convenience we have divided these into two groups:

Chemical Experiments.		*Excretion of Drugs.*
Important reactions of:	Methanamine	Phosphate, etc., in the urine
	Formaldehyde	Iodine in the saliva
	Alcohols	Physical chemistry of soaps and emulsions
	Phenols	Action of indicators, U. S. P., etc.
	Salicylates	Buffer value of phosphates

Antiseptics
  Phenol co-efficient, etc.
  Common uses
Astringents
  Effects on tissues
Effects of acids and alkalies
  On protein
  On mucous membrane
Preparation of colloidal solution gels
  Importance in drug action

Physiological Experiments.

Irritants and demulcents
  On skin and mucous membrane
  Local anesthesia on a frog
  Local anesthesia on a man
Administration of anesthetics (rabbit)
  Ether
  Chloroform
  Chloral hydrate
Magnesium sulphate
Effects of (rabbit)
  Morphine
  Chloroform
  Chloral hydrate
  Magnesium sulphate
Action of: (frog, guinea pig and cat)
  Digitalis
  Atropine
  Pilocarpine
Effect of drugs on circulation (dog or rabbit)
  Demonstration
Effects of drugs on G. I. tract (rabbit)
  Demonstration

This course will be given throughout the senior year and will be supported by the courses in Dispensing. The course as originally given will be continued for graduate study.

I am certain that the work which we have been giving during the past four years has enabled our students to have a better understanding of the whole field of therapeutics. It has impressed upon them the need for care in preparing sterile solutions for hypodermic injections, intravenous use of glucose, and an accurate physiological salt solution.

They know why a doctor prescribes an Eggleston dose of digitalis, because they have seen its action in an animal. They understand the normal functions of the human body better, and are, therefore, entitled to be considered by the physician as an indispensable aide in his service to the patient.

THE INTER-RELATION OF THE DEPARTMENTS OF PHARMACOGNOSY, PHARMACOLOGY AND CHEMISTRY.

Editor's Note: Education should not come in separate "packages" wrapped and labeled, chemistry, pharmacy, pharmacology, etc., because all of these subjects are inter-dependent and should dovetail with each other. This dovetailing cannot be successfully done without an effort on the part of the instructors. Professor Christensen points the way for such coöperative efforts.—C. B. JORDAN.

BY B. V. CHRISTENSEN.*

Inasmuch as this paper is to be presented before a group of teachers of chemistry it is presumed that you will be interested in a few suggestions pertaining to the chemical training of students deemed desirable by teachers of pharmacognosy and pharmacology. The suggestions offered herewith relate more particularly to the nature rather than the scope of chemical knowledge which teachers of pharmacognosy and pharmacology consider essential as aids to a proper understanding and appreciation of these subjects by students. As a matter of fact, if you would

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permit a criticism, I would say that your weakness lies in quality rather than quantity. However, inasmuch as the writer is not a chemist, this discussion is not to be considered a critical review of the teaching of chemistry. It is intended only to offer a few suggestions as to the nature of the chemical knowledge which is of particular value to students in acquiring an understanding and appreciation of the subject matter of pharmacognosy and pharmacology. No attempt is made herewith to classify chemistry under its various subdivisions such as inorganic, organic, physical, etc., and especially in view of the fact that some of the suggestions offered might apply to all or any one of the various subdivisions.

INTERPRETATION OF CHEMICAL LANGUAGE.

First and foremost, we should like to have students well trained in the reading of and interpretation of chemical language. A chemical equation, for instance, is a statement of a chemical fact or theory. As a matter of fact, in many cases a chemical equation is a paragraph or a page of information to those who know how to read and interpret. Take, for instance, the simple equation, $NaOH + HCl = NaCl + H_2O$. If this is true, it tells us that one molecule of sodium hydroxide will combine with one molecule of hydrochloric acid to form one molecule of salt and one molecule of water. It also tells us that 40 Gm. of sodium hydroxide will combine with 36.5 Gm. of hydrochloric acid to form 58.5 Gm. of salt and 18 Gm. of water. We might use Mg or pounds or tons in the same proportion. Again it may tell us that the valence of chlorine is one, of oxygen two, of sodium one and so on. This is simple, of course, but illustrates the point in mind.

A chemical formula also should convey considerable information to a student. From it he should be able to classify the compound as an alcohol, aldehyde, alkaloid or whatever it may be. He should also be able to predict stability and reactivity and, the nature of compounds formed as a result of the reaction, *i. e.*, he should be able to predict polymerization, addition or substitution. He should be able to predict at what point the reaction might occur and thus suggest possible new compounds and the nature of such as for instance, the barbiturates.

We expect students to know at least the elementary principles of nomenclature so that they will recognize the same substances under different chemical names and so that from a given formula they may derive a correct chemical name. This also applies to ide, ate, ite, ic and us endings. We expect also that students know enough about isomerism to appreciate why it is that two substances may have the same empirical formula and yet differ as to physical properties and physiological action.

From the above viewpoint we might compare chemistry to a new language, and proficiency in chemistry, therefore, depends to a large extent upon the quality and scope of the chemical vocabulary of the student.

NATURE OF SUBSTANCES.

Second, we should like to have students come to us well informed as to the nature of substances. They should appreciate thoroughly that substances are recognized and differentiated by means of their properties, both physical and chemical. Students should have clear and definite knowledge as to the meaning and significance of specific gravity, melting point, boiling point, solubility, optical rotation,

refraction, etc. When he is told that the specific gravity of a substance is 2.3 at 4° C., he should be able to determine the weight of a given volume of that substance. When given weight and volume, he should be able to determine specific gravity and when given specific gravity and weight he should be able to determine volume. We expect students to know the nature of such substances as fats, fixed oils, carbohydrates, glucosides and gums. I mention these particularly for the reason that in my experience these have offered the greatest difficulties. It is not enough for students to know that fixed oils are made up fundamentally of glycerides of fatty acids but they should know the nature of the more common glycerides such as olein, linolein, palmitin, etc. Are these glycerides liquids or solids, how do they differ as to consistency, melting point, color and other pertinent properties? If the students know the nature of the more common glycerides, they have less difficulty in understanding and appreciating why we have several fats and fixed oils official and how they differ from each other.

With respect to the nature of substances, qualitative tests should not be overlooked. Students should be trained in the use and application of such tests in recognition and differentiation of substances. Finally, we expect students to be able to make quantitative determinations both gravimetric and volumetric and, in this connection, we suggest that students not only be carefully instructed but drilled on the meaning of the various terms used in connection with volumetric solutions, such as normal, tenth-normal, half-normal, etc., and considerable practice be required in preparing and standardizing such solutions.

PROCESSES.

Third and last, we expect students to have a knowledge of processes. For instance, students should be proficient in performance of the various processes used in determining specific gravity for the several types of substances such as those insoluble in and heavier than water, insoluble in and lighter than water, substances soluble in water and for which some other liquid must be used, liquids, powdered or granular substances and so on. We expect them to know how to determine melting point, boiling point, optical rotation and solubility. Again, students should be able to purify substances by crystallization or sublimation or fractional distillation or by selected solvents. They should understand the differences between direct steam distillation, indirect steam distillation, destructive distillation, fractional distillation, distillation under reduced pressure and the principles underlying each process.

In closing allow me to state that I appreciate the fact that you are not teaching your students fundamentally for the purpose of preparing them for pharmacognosy and pharmacology. However, it does appear that you are training your students for future needs, some of which occur during their college life. Hence, if the students need the foundation in chemistry outlined above, it seems logical that their courses in chemistry should include such instruction both as to character and scope of information. Let me remind you again, that as far as pharmacognosy and pharmacology are concerned, it is desirable to emphasize quality rather than quantity of chemical information.

Eighty-second annual meeting of AMERICAN PHARMACEUTICAL ASSOCIATION and dedication of the American Institute of Pharmacy during week of May 7th. See Transportation under department "Societies and Colleges."

THE CONFERENCE OF PHARMACEUTICAL LAW ENFORCEMENT OFFICIALS

MINUTES OF THE SESSIONS HELD IN HOTEL LORAINE, MADISON, WIS., AUGUST 31 AND SEPTEMBER 1, 1933.

The fifth annual meeting of the Conference of Pharmaceutical Law Enforcement Officials was convened by Chairman R. L. Swain, at 9:00 A.M. in the Colonial Room, with the following present: Messrs. H. H. Schaefer and F. C. A. Schaefer, of New York; Pierce, of Maine; McShane, of Vermont; Jones, of South Dakota; Childs, Milne, King and Reese, of Kansas; Hayman, of West Virginia; Bingham, of Alabama; Meads, Teeters, Slocum, Judisch, of Iowa; Hankins, of Florida; Costello, of North Dakota; Henry, Durham, of Michigan; Fischelis, of New Jersey; Nye, of Missouri; Monias and Christensen, of Illinois; Netz, Bender, of Minnesota; Wilson, of Georgia; McCullough, Russell, of Indiana; Wilcox, of Pennsylvania; Philip, California; Jelinek, of Minnesota; Kremers, of Wisconsin; Kelly, Eberle and Swain, of Maryland, Ford, of Ohio.

Chairman Swain delivered his address and upon motion duly seconded, same was received for publication.

THE CHAIRMAN'S ADDRESS.

BY R. L. SWAIN.

In presenting this address to the Conference of Pharmaceutical Law Enforcement Officials, I shall endeavor to establish one or two general propositions to which I think we should devote our earnest thought. First of all, I think it is our responsibility to point out the defects existing in the pharmacy laws, and to take the lead in having these defects corrected. Secondly, we should do all that we can, in our official capacity, to acquaint the public with the basic significance of pharmacy to public health. I couple these two thoughts together because I am not able to see any way of correcting the defects in pharmaceutical legislation unless our efforts are based upon the public function which pharmacy renders. The whole field of drugs and medicines is so closely connected with the public welfare that pharmaceutical legislation should seek to lodge its regulation and control with the pharmaceutical profession. I have no difficulty in feeling that proper and adequate pharmaceutical legislation is a logical and certain outcome of a due regard, on the part of the public, of the work which pharmacy does.

Assuming that these propositions are sound, and I doubt that any will contend against them, then it seems to me that enforcement agencies should carefully study existing laws, with the view of evaluating their effects upon the community.

Legislation, restricting the practice of pharmacy and the distribution of drugs and medicines to persons meeting lawfully established standards of education and experience, has long been a part of the public general laws of every state. The constitutionality of this legislation is no longer open to question. It is well established that such restrictive regulation and control is a proper exercise of the police power of the states. The police power of a state is the inherent sovereign authority under which its legislature may, within constitutional limits, prescribe the laws and regulations to safeguard the safety, health and morals of the people, prevent fraud and oppression, and promote the public convenience, prosperity and general welfare.

The purpose of these laws is to surround the distribution of drugs and medicines with certain definite legal precautions. Competency and skill are required of those seeking to engage in this important activity.

However, a casual study of the pharmacy laws discloses some major defects. While they do set up generally satisfactory standards for purely professional pharmaceutical practice, all of them recognize certain exceptions and exemptions which go far to defeat their public purpose. As a very general rule, pharmacy laws permit the free and unlimited sale of patent and proprietary medicines and the commonly used household or domestic remedies. True, the language varies, but the meaning and import are the same. This condition is far from new. It seems to have been coexistent with pharmaceutical legislation in this country. The first pharmacy law enacted in this

country was, so far as I have been able to learn, passed in South Carolina in 1817. Among its interesting provisions, was one stating that it should not apply to the sale of home-made remedies and such as were obtained from manufacturers in shape for lay use. From that early day, no pharmacy law has been passed without making liberal exceptions in behalf of patent and proprietary medicines.

It should be admitted, I think that there was once some valid basis for the exceptions. Drug stores were not as easily accessible as they are now, and hence, general dealers were permitted to handle drugs and medicines. Transportation and the lack of the modern means of communication also had to be taken into consideration when legislation of this type was being considered. Also the pharmacist or druggist was not accepted as an educated man. In those early days, he was a merchant, carrying drugs and medicines as a side-line. As a logical result, drugs and medicines were looked upon simply as articles of merchandise, and as such, could be handled without restriction or control. This view finds recognition in early court decisions, in which all attempts at restriction were set aside. Being mere articles of merchandise, no reason was acceptable to justify permitting their sale by some and prohibiting it to others. Under the light of changed conditions, we may well question the wisdom of perpetuating the old points of view. For instance, good roads, telephones, automobiles have annihilated distance, and the drug store is, in most sections of this country, convenient to the people. Also, the pharmacist is now a man of college and university training, and well qualified to serve the public in a professional capacity and to advise in the use of drugs and medicines. Also, such salutary legislation as the Food and Drugs Acts has done much to drive the merchandise conception out of medicine, and to reserve the field for such preparations as are reasonably safe. Drugs and medicines are more and more becoming health adjuncts and thus perhaps more definitely belonging in the hands of persons of training and experience. The final report of the Committee on the Costs of Medical Care has focused attention upon medical problems, and has made the specific recommendation that the standardization, preparation and distribution of drugs and medicines be restricted to pharmacists in so far as this is possible and practicable.

It would be possible to record other changes which have come about, and to show that the old bases of the exceptions no longer exist. However, perhaps the most significant development in the whole matter, and the one deserving of the most careful study at our hands, has been in the nature of the products which may be defined as proprietary. I think it can be said that the early use of the terms, patent and proprietary medicines, was in keeping with the general accepted meaning of the terms. While the words were "patent and proprietary medicines," the phrase had no implications beyond the usual patent medicine. The word, "proprietary," was synonymous with and descriptive of the word, "patent." Thus a proprietary medicine was no more than a patent medicine. That the conditions have changed is quite obvious. There has long been a marked drift away from manufacturing in drug stores, and to a concentration of production in the large pharmaceutical manufacturing plants. Concurrent with this change has come about the pharmaceutical specialty under special trade-marked names. Many complex and potent preparations can be obtained under short and easily remembered names. The great research laboratories of the pharmaceutical and chemical plants are turning out a continuous and ever-growing list of special preparations, the property rights to which are owned by the companies themselves. The chemo-therapy age, which now exists, is bending its every energy to the production of specialties for the treatment of disease. In most cases, these products are complex, potent, frequently dangerous and are invariably obtainable under short trade names. While these products vary tremendously in their nature, use, toxicity and adaptability to disease, they are all alike in that they are "proprietary products." Some concern has a property or proprietary right to the patent under which they are produced, and to the name and package in which they are sold. Thus, in an important sense, as soon as the most dangerous research product becomes available to the public, it also comes to the public as a "proprietary" product or medicine. There may be little general knowledge regarding it; the medical profession may consider it as in the experimental stage; the public may be totally unacquainted with it, and yet, under the pharmacy laws themselves, enacted in the public interest, such products may be handled and sold by anyone, irrespective of skill and training. In other words, the exceptions in the pharmacy laws still make it possible for the most dangerous products to be distributed to the public as merchandise.

To show the absurdity of the present conditions, it can be said that in one state camphor-

ated oil may be sold only by a registered pharmacist, while veronal, barbital, amytal and many others may be sold by anyone. In most states, no distinction is practiced, and patent and proprietary products and the usual domestic remedies are freely available from any and all kinds of retail dealers. The mere fact that the evident and obvious legislative intent was to permit free sale of patent medicines and the commonly used household remedies has not prevented dangerous proprietary preparations from being just as freely sold and distributed.

It must be apparent to all that such a condition is certainly not in the public interest. In fact, it seems greatly inconsistent with the main purpose of all pharmaceutical legislation.

As I see the matter, our whole system of pharmacy laws should be carefully studied. Many of the provisions should be entirely rewritten. An intelligent and earnest effort should be made to make them more stringent, and thus more effective. The broad, general exceptions in favor of general merchants should be removed and reconsidered in the light of prevailing needs and prevailing conditions.

I urge, as a beginning, that the Conference approve the appointment of a committee to carefully study the significance of the terms, "proprietary preparations" and "patent medicines," so that these may be defined in the light of present scientific knowledge, and with due regard to the demands of public health.

Upon motion of Mr. Childs, seconded by Mr. Milne, a motion was adopted that the incoming chairman appoint a committee to draft a suitable definition for patent and proprietary medicines.

Secretary and Treasurer M. N. Ford, of Ohio, presented his report as follows:

THE REPORT OF THE SECRETARY-TREASURER.

BY M. N. FORD.

Since the last annual meeting of the Conference of Pharmaceutical Law Enforcement Officials, your chairman, Mr. Swain and the secretary, have had numerous requests for information regarding enforcement of pharmaceutical laws and to each request, we have lent all possible aid.

On December 17, 1932, upon the request of Chairman Swain, we sent a letter to each Secretary of every State Board of Pharmacy as well as other departments having to do with pharmaceutical law enforcement, with regard to the sale of drugs and medicines by vending or slot machines. From the response that we had, it seems the letter was very timely in that a number of states have sought opinions and amendments to the law that would bar the distribution of drugs and medicines through vending machines.

On January 31, 1933, Chairman Swain also directed me to send a letter to all State Boards of Pharmacy, as well as other state departments having to do with pharmaceutical law enforcement, the letter dealing with amending the pharmacy laws to use the term "packaged medicines" in preference to the term "patent or proprietary medicines." The fact that the exemption clause of the law permitting the sale of patent or proprietary medicines by general dealers is sufficiently broad, we should exert every energy to see that the law is not changed to grant further exceptions.

We received numerous acknowledgments of receipt of this letter and assurance that no such legislation proposed would be sanctioned by enforcement officials.

The report of our last annual conference as you know, appeared in the JOURNAL OF THE AMERICAN PHARMACEUTICAL ASSOCIATION in the December issue and contained thirty-one pages of printed matter, and on February 17th, we obtained 300 reprints of the proceedings which were mailed out as first class mail, to the members of the Boards of Pharmacy, as well as others interested in pharmaceutical law enforcement.

On February 21st, we wrote to all the secretaries of the State Boards of Pharmacy, as well as other pharmaceutical law enforcement officials, regarding the annual five-dollar contribution to the Conference. This request was followed up by a letter on June 8th, and up to this time, the following 25 states have contributed the usual five-dollar fee. I list the states in the order in which the fees were received:

Ohio, Indiana, North Dakota, Kentucky, Colorado, New Jersey, Iowa, Georgia, West Virginia, New York, Alabama, Maryland, Pennsylvania, Arkansas, Michigan, Delaware, New Mexico, Kansas, Vermont, Oregon, Florida, Idaho, South Dakota, Minnesota and Wisconsin.

In addition to those already contributing, we have had acknowledgments from some of the States, stating their contributions would follow a little later on.

FINANCES.

Receipts.

Balance on Hand	$243.94
Receipts from 25 states at $5.00 each	125.00
	$368.94

Disbursements.

12/29/32 to L. A. Engel, letter heads and reprints	$ 7.50	
2/17/33 Postage for Secretary's office	50.00	
3/18/33 to JOURNAL A. PH. A. printing proceedings	115.77	
8/15/33 to Dr. R. P. Fischelis for work on Synonyms report	25.00	
Total Disbursements	$198.27	
Total Cash Balance		$170.67

Upon motion of Mr. Milne seconded by Mr. Costello, the report was approved.

Upon motion of Mr. Childs, seconded by Mr. F. C. A. Schaefer, the Chairman was to appoint a Finance Committee of five to provide for the finances of the Conference in the future.

At this time the Chairman called upon Secretary Kelly of the AMERICAN PHARMACEUTICAL ASSOCIATION and his remarks concerning the Conference were very encouraging and greatly appreciated.

Chairman Swain next called upon Walter F. Meads of Iowa for a paper upon "The Value of Annual Renewal of Pharmacists' Certificates in the Enforcement of Pharmacy Laws." The paper was received and discussed by Messrs Fischelis, Pierce, Henry, Hankins and Swain.

THE VALUE OF ANNUAL RENEWAL OF PHARMACISTS' CERTIFICATES IN THE ENFORCEMENT OF PHARMACY LAWS.

BY WALTER F. MEADS.

In presenting this paper at this session of the Conference of Law Enforcement Officials, I will attempt to show you the analogy between the annual renewal of the pharmacists' license and law enforcement. How in the State of Iowa, with whose workings I am most familiar, the enforcing of laws governing the practice of pharmacy is dependent on, or closely allied to, the renewal of certificates.

In 1880, the first pharmacy law was enacted in Iowa. It provided regulations for the sale and distribution of drugs and medicines, as well as for the establishment of a commission of pharmacy, which was given authority to administer the affairs of the profession. This included the enforcement of the laws governing the practice of pharmacy and the licensing of pharmacists by examination.

In order to place the profession and the distribution of drugs and poisons under State regulation, with its added protection to the druggists and to public health, it was agreed by the pharmacists that the expenses of the department and of the law enforcement would be paid through the collection of license fees and the annual renewal of certificates. That this was a wise agreement can be shown by the benefits accruing from the annual renewal of certificates.

The greatest value of the annual renewal is perhaps that it provides funds for law enforcement which might be obtained if the Board was dependent entirely upon funds raised by a general taxation. While it is true that the money we collect is paid into the State Treasury and an appropriation must be made by the legislature for our expenses, the fact that the Board is more than self-sustaining is a valuable argument when requesting funds for the operation of the department. This has also been a valuable argument, when on several occasions, the pharmacy board has been faced with consolidation. The fees are largely responsible, I believe, for the fact that we have always been independent and have held the administration and enforcement of the pharmacy laws in the hands of members of the profession, the value of this independence can be appreciated by all of us here.

It was the provision of the annual renewal and its ensuing independence that placed the

pharmacists in Iowa in the position of being able to secure in 1885, a law governing Itinerant Vendors of Medicine, requiring an annual license fee. This law is still in effect and enforced by the Iowa Pharmacy Board. We have been very fortunate in retaining the administration of this law, for such regulations are best enforced by those who are directly interested. We have not only given our own druggists protection from this type of competition, but have added considerable to our prestige, by turning back to the State General Fund the sum of $20,000 to $40,000 a year. Over the period of years the grand total above expenses, is something over $900,000.

The annual renewal of certificates is of assistance to us in law enforcement, in that the information requested on the renewal application blank gives us a record of the pharmacist which can be obtained otherwise only by personal contact. This application when returned with the fee for renewal, gives the location of the pharmacist, whether active in retail drug business or not, and if active whether it be as proprietor, manager or clerk, as well as the name of the firm where he is practicing. Some states have sufficient inspectors to call in all stores several times a year, but we are not so fortunate in this respect. Through our renewal we check by mail as it were, the things an inspector would learn through a visit to the store as our files are our check when any violations are reported, relative to the supervision of licensed pharmacists in drug stores. It is our policy as a rule, to send out each year with the renewal receipts, notices of changes in laws, reports or request for coöperation along the line of law enforcement. This has brought big returns in interest and a closer contact with the druggists over the state. Through this closer touch, they feel that the work of the Pharmacy Board, including law enforcement, is part of their own personal responsibility. Other states can and do send out material of this nature, but the renewal is an easy and natural way to handle this type of work which is one of the duties of the Pharmacy Board.

In the inspection of drug stores the work is facilitated by renewal receipt card, which in Iowa must be on display along with the original license. The inspector can tell at a glance whether the certificate is in good standing and if not, a check is made to ascertain whether the owner is active in the store, or the reason for failure to renew the license.

I hope I have successfully pointed out to you, why we in Iowa feel that the annual renewal of certificates is of considerable value in the enforcement of the laws coming within the jurisdiction of the Pharmacy Board. To sum up, *first*, because it brings in funds not raised by general taxation, with which to best administer the pharmacy laws in the interest of public health and the profession. *Second*, because through annual renewals it is possible to keep in closer contact with the pharmacists, thus we have the opportunity to give as well as receive information relative to law enforcement. *Third*, the establishment of a feeling of coöperation by regular contact between the department and the licensed pharmacist over the state.

Dr. R. P. Fischelis next presented his paper on "A Legislative Attempt to Establish Prescription Tolerances." The paper was discussed by Messrs. Meads, Durham, Hayman and Hugo Schaefer.

A LEGISLATIVE ATTEMPT TO ESTABLISH PRESCRIPTION TOLERANCES.

BY ROBERT P. FISCHELIS.

A law recently passed in New Jersey and known as Chapter 309, P. L. 1933, regulates the compounding of prescriptions. Its principal provisions are as follows:

(1) It is made unlawful for any person who is not a registered pharmacist to compound, dispense, fill or sell prescriptions of licensed physicians, dentists, veterinarians or any other licensed medical practitioner.

(2) Apprentices employed in a pharmacy may compound, dispense, fill or sell prescriptions of licensed physicians, dentists, veterinarians or any other licensed medical practitioner under the immediate personal supervision of a registered pharmacist.

(3) A prescription is an order for drugs or medicines or combinations or mixtures thereof, written or signed by a duly licensed physician, dentist, veterinarian or other licensed medical practitioner.

(4) Prescriptions of licensed physicians, dentists, veterinarians or other licensed medical practitioners transmitted by word of mouth, telephone, telegraph or other means of communication must be recorded in writing by the pharmacist, and the record so made constitutes the original prescription which must be filed as indicated below.

(5) Every registered pharmacist compounding, dispensing, filling or selling a prescription must place the original written prescription or the prescription as recorded by the pharmacist, in case of telephoned, telegraphed or other communicated orders from practitioners, in a file kept for that purpose.

(6) The registered pharmacist must affix to the container of every prescription dispensed a label bearing the name and address of the pharmacist, the date on which the prescription was compounded and an identifying number under which the prescription is recorded in his files. The label must also bear the name of the licensed practitioner writing or communicating the prescription and the directions for the use of the prescription by the patient, as directed by the licensed prescriber.

(7) It is a violation of the Act if a prescription is found to contain more or less than the quantity of the several or combined ingredients ordered by the prescriber.

(8) It is a violation of this Act if the prescription contains ingredients other than those ordered in writing by the prescriber. The addition of such inert ingredients as are required in the art of compounding is permissible when such ingredients are not used in any manner to replace the several or combined constituents ordered by the prescriber. No replacements can be made without the prescriber's permission.

The final weight or volume of a prescription must not be more or less than the original prescription calls for. The quantities of individual ingredients must not deviate from the weights or volumes prescribed. A reasonable tolerance may be permitted to account for manipulative procedures and normal variations due to unaccountability for accurate weighing and measuring and for the use of drugs of standard strength as well as for strict accuracy in all operations involving subdivision of bulk quantities into the individual doses prescribed. "Eye measurements" in subdividing capsules, powders and similar dosage forms are not to be relied upon in place of accurate weighing and measuring devices.

(9) The Board of Pharmacy has the power to make rules and regulations for the enforcement of this act and is authorized to establish tolerances to allow for deviations from the amounts of ingredients prescribed due to manipulative procedure or deterioration.

(10) All violations of this act are punishable by penalties ranging from a minimum of $25 for the first offense to $100 for third and subsequent offenses.

We believe this to be the first State law which specifically grants authority to a Board of Pharmacy to establish tolerances for prescription work.

Rowland Jones, of South Dakota, next presented a paper on "What Privileges Should Be Granted the Unregistered Dealer under the Pharmacy Laws?' The paper was received and discussed by Messrs. Fischelis, Monias, Wilson, McCullough and Philip.

WHAT PRIVILEGES SHOULD BE GRANTED THE UNREGISTERED DEALER UNDER THE PHARMACY LAWS?

BY ROWLAND JONES, JR.

The question of what privileges should be granted unregistered dealers under the pharmacy laws is indeed an important and vexatious one. The pharmacy laws of the forty-eight states differ in wide range in the treatment of this problem. Examination of pharmacy laws of the various states indicate that we have an almost complete absence of uniformity in the methods evolved in the treatment of the evils these laws were designed to mitigate. The laws of the several states extend in scope from almost complete freedom from restraint of the unregistered dealer, as embodied in the six- and ten-mile qualifications in some states to rigid restriction on nearly all drug products in others.

For the reason that my experience in pharmacy law enforcement and the development of changes in pharmacy laws in general has been limited to a strictly agricultural area in which comparatively long distances separate registered pharmacies, I shall treat the subject in the light of such experience and depend upon subsequent discussion by the group to develop the phases of the problems as they exist in more thickly settled and in urban districts.

In South Dakota, the evolution of the pharmacy laws since statehood was attained in 1888, has been confined to the last six years. As in many states the territorial pharmacy law, which was usually written by pharmacists, was carried into the statutes subsequent to admission

to the union. This law was drawn in such a manner as to definitely restrict practically all drugs and medicinal preparations to the pharmacist. It is regrettable that during this period of rugged individualism, which now seems definitely on the wane, the opinions arising therefrom were reflected in the decisions of the courts of the states in such manner that the law was emasculated by the "original package" decisions as was the case in many states. There can be no questions that these decisions made by courts, to whom the merest whisper of monopoly was abhorrent, resulted in enormous diversion in the sale of drug products into channels foreign to pharmacy. It is also true that these decisions which left glaring defects in pharmacy laws generally, resulted in strong efforts to correct some of the evils arising therefrom. Such efforts have met with varying success in the different states.

In South Dakota in 1927, a case was carried to the state supreme court upon the question of the constitutionality of the pharmacy law controlling the sale of patent and proprietary medicines in original packages which resulted in what we know as the Wood's Decision. This decision held that a section of the pharmacy law was unconstitutional in its restriction of the sale of patent and proprietary medicines in original packages to the pharmacist. This decision immediately resulted in a great deal of confusion and difficulty in the administration of the law by the Board of Pharmacy for the reason that the average mind of the layman seemed unable to differentiate between patent and non-patent preparations and between poisonous and non-poisonous proprietary preparations. Cases were lost which involved the sale of U. S. P. and of poisonous preparations through the erroneous applications of the "original package" formula laid down by the Supreme court. This condition became so serious that it became necessary to go to the legislature for relief.

As a result a patent and proprietary medicine license law was enacted early in 1933 without difficulty. This law was in the form of an amendment to that section of the law declared unconstitutional in the Wood's case and had the effect of curing the constitutional defect but which at the same time regained the elements which had been indirectly lost. The amendment provided that any merchant operating an established place of business (eliminating itinerant vendors) might apply to the Board of Pharmacy for a license to sell patent and proprietary medicines. The fee of $3 is retained by the Board for the purposes of inspection and general pharmacy law enforcement. In this amendment we defined patent and proprietary medicines as follows: "any medicine or drug which is prepared or compounded in proprietary form and sold in original packages, where the sale thereof is *unregulated under the laws of the state.*" Thereby, in one step, we eliminated the decision of the supreme court in the Wood's case as a precedent for the reason that we cured the defect in the law as pointed out in that decision and at the same time, brought the sale of these products back under our control. This definition, which had had no existence in statute before this time, resulted in a clarification of the statute on the dividing line between patent and proprietary medicines on the one hand, and U. S. P. and poisonous preparations on the other, the latter classification being adequately covered in the original law. Therefore, U. S. P. drugs and preparations and poisonous products may not be sold in other than registered pharmacies in South Dakota. We do not feel that any privilege whatsoever should be granted to unregistered dealers in these classifications.

Another result which has been advantageous in the enforcement of the pharmacy laws is the provision for the cancellation of the patent and proprietary licenses upon evidence of law violation. This gives the Board of Pharmacy a potent weapon in the fight for restrictions on the sale of drugs and medicines.

At the time when this legislation was being considered it was said by some that such a license would result in great multiplication of the outlets handling patent and proprietary preparations. The fact, as now established, is that a large number of small dealers such as restaurants, filling stations, billiard parlors, hardware dealers and grocers, who in the past have carried small stocks of these preparations have discontinued the sale of these rather than take out the license. In many places no licenses have been applied for while in the smaller towns without pharmaceutical service, the license has resulted in a quieting of the demand for more privileges for the unregistered dealer which is a force to be reckoned with at every session of the legislature.

As for the six- and ten-mile laws which have been passed in some states, I hold the opinion that this is bad law from the standpoint of pharmacy. From the standpoint of public health no differentiation in restrictions on this basis is even reasonable, and surely the public in the communi-

ties affected will lose sight of the importance of adequate pharmaceutical service. Also the prospective student of pharmacy will not be encouraged by the picture presented under such a system.

During the past ten years we have witnessed a gradual but distinct retrogression in the statutory protection of the field of pharmacy, mainly through judicial decisions, and during the same period we have advanced rapidly in educational facilities and requirements for the pharmacist. If this retrogression continues to such an extent that legal protection on U. S. P. drugs and preparations and poisons is lost as we have lost the protection in the patent and proprietary field, I feel grave concern as to our ability to maintain pharmacy at its present high level.

I believe, that as pharmacy law enforcement officials, it behooves us to oppose to the limit further modification of pharmacy law restrictions and to work toward licensing restrictions upon sales of drug products through other outlets. While in South Dakota, we were forced to accept a license fee of only $3 for the patent license, I believe that such license should be much higher. It would seem from the taxation standpoint, that the license for the sale of patent medicines should be at least as high as that required for the sale of non-intoxicating beverages.

Where funds for law enforcement are needed by Boards of Pharmacy, license fees should be allocated directly to the Boards for this work. Where funds are ample such license fee may be advanced as a source of tax income to the state which is badly needed in most states. Needless to say, the latter course offers a valuable lever in a successful legislative campaign.

The sale of biological products presents a problem, particularly in parts of the country where the treatment of veterinary diseases provides a lucrative source of income for the pharmacist. In many states such products are freely sold without restriction and even in some cases by itinerant vendors. The proper storage and handling of biological products and their intelligent dispensing is important. Biologicals for veterinary use have a definite public health relation. Ignorant use of biologicals constitutes a menace if handled without benefit of expert knowledge. Most pharmacy laws define drugs and medicines using the term "for man or for animal." With this in mind we have ample ground for insisting that the sale of veterinary biologicals by other than licensed veterinarians be restricted to the pharmacist. For example, the average uninformed storekeeper should not have the privilege of keeping for sale anthrax live spore vaccine.

In the field of insecticides and fungicides it seems evident, that we as pharmacists, cannot hope to control the general sale of such products which have become staple articles of commerce. I believe, however, that such sales by unregistered dealers should be accompanied by such regulations as license, registration of sales, labeling, etc. The pharmacist who will keep himself informed upon the technical aspects of this rapidly growing field, need have little fear from competitive outlets.

This paper is possibly misnamed. It should be "What Privileges Should *Not* Be Granted Unregistered Dealers." It is my contention that no privileges, with the exception of those herein discussed, should be granted in any case without a strenuous fight. If the sale of drugs which have been termed "simple household medicines" by those seeking to undermine pharmacy statutes, is allowed by unregistered dealers, it will only serve as an entering wedge and such action will be made a basis and a precedent for further encroachments.

U. S. P. drugs and preparations have always been and are now strictly within the field of pharmacy as have been poisons, with the exceptions heretofore noted. Let us be prepared to fight for that which is rightfully within the province of pharmacy and not grant privileges to laymen, the demand for which has so greatly increased due to the stringency of economic conditions. Without strict statutory protection, pharmacy as we know it and as we dream it for the future, cannot continue its logical progress. The health of the nations needs this progress.

Mr. Mac Childs of Kansas next gave an address verbally on the "Need for Strict Enforcement of Law," in which he suggested the Conference follow the method of the N. A. B. P. as to model laws for enforcement. The subject was discussed by Messrs. Meads, Judisch, Fischelis, Durham, Swain and Henry. An excerpt follows:

THE NEED FOR STRICT ENFORCEMENT OF THE LAW.

BY MAC CHILDS.

"My speech is going to be a series of recommendations rather than the discussion assigned. The National Association Boards of Pharmacy was the conceived idea of several gentlemen and has

done great work. It has served its purpose admirably and I think in the next five years will complete what it set out to do, and I hope it will be of greater help to the different parts of the organization which wish to make their laws more stringent and more useful. Each of us have ideas that should constitute our laws, but the trouble is that we have local ideas and we usually have a local law. I have found that in cases of court that the citing of a precedent established in another state is a very great help in clinching the case as the judge and jury usually use the precedent set. I might say that I have also found out that the enforcement must be tempered and not too strict as it is primarily for the protection of the public and of course it reverts back very favorably to the pharmacists.

"At one time, three years ago, I was Secretary of our Board and thought maybe we had better 'clean-up our own back yard' first. We made an inspection of every drug store in Kansas and we notified druggists as to where they were making a violation and notified them that the inspectors would call on them in two or three weeks. We requested them to send in a notice to the Secretary of the Board that this violation had been eliminated and it would not be continued. Of course, in a great many instances we found that their reply was just like the advertising of many patent medicines, it was 'baloney.' In some cases warrants were sworn out and we received 100% convictions. We do not believe convictions are the way to handle this, but with certain people this is necessary. After 'the clean-up in our own back yard' we had very little trouble with others. We treated everybody alike. I was condemned a lot at first and lost many of my friends, who thought I was picking on them. After they found they were receiving the same treatment as anyone else they have become my very good friends again and have given me much help. We made some mistakes in our law enforcement by trying to be over zealous. We tried to stop the sale of paregoric by unregistered pharmacists and only by prescription of physicians. We, later, found out that there was a legal use for a 2-oz. bottle of paregoric and found that we had made a mistake in allowing it to be sold only by a physician's prescription; as we had given them something these should not have left our control."

The speaker also described how they handled their court cases and said they did not even take a case into court unless they were positive they could get a conviction on it. They usually got an opinion from the Attorney General, and had this opinion read in the court the case was being tried or else had an Asst. Attorney General present. He also said that to have the proper evidence that prescriptions were being filled by a person not under the direct supervision of a registered pharmacist it was necessary that the inspector catch him in the act and actually see that this was done or else the evidence would not stand up in court.

Hugo H. Schaefer, in the absence of Mr. Mather, presented the subject, "Restricting the Practice of Pharmacy to Proper Persons." The subject was then discussed by different members, until 12:15 when the Conference adjourned.

Thursday, August 31, 1933.

At eight P.M. a joint session was held in the Pompeian Room with the Section on Education and Legislation. The joint session was well attended and it was urged the annual joint sessions be continued.

Friday, September 1, 1933.

The Conference convened at 2:00 P.M. in the Colonial Room with the following present: Messrs. Fischelis of New Jersey, Costello of North Dakota, Mr. and Mrs. Bruce Philip of California, Henry, Durham and Borniac of Michigan, Heine of Texas, Hugo H. Schaefer and F. C. A. Schaefer of New York, Monias of Illinois, King and Milne of Kansas, Teeters of Iowa, Rothrock of Indiana, Swain of Maryland, King and Ford of Ohio.

Chairman Swain asked for the presentation of the paper of Mr. Woodside of Pennsylvania on the subject "A Change in the Law Enforcement Procedure in Pennsylvania." In the absence of Mr. Woodside, the paper was presented by Hugo H. Schaefer of New York. Upon motion of Mr. Henry seconded by Mr. Schaefer, the paper was accepted and discussed.

A NEW SYSTEM OF LAW ENFORCEMENT IN PENNSYLVANIA.

BY JOHN M. WOODSIDE.*

New deals in governmental procedure are so common at present that it seemed reasonable to expect, in some states at least, a change in the manner of enforcing the pharmacy laws.

* Enforcement executive, Pennsylvania Board of Pharmacy.

When changes have taken place they have been due to one of two reasons, either dissatisfaction with the former system or they were prompted by an economic situation.

No administrative agency is free of criticism of its enforcement of laws coming within its jurisdiction and no new system will eliminate this entirely for no law beginning with the Ten Commandments inscribed on the tables of stone by Moses, have been enforced to the satisfaction of every one.

In Pennsylvania the Board has had the usual amount of dissatisfaction but the change in the manner of enforcing the Pharmacy Laws was brought about through an economic reason. The change did not originate with the Board but was instigated within the Department of Public Instruction in which the Board of Pharmacy and all other professional Boards are units. Previous to September 1932, the Board of Pharmacy was allotted two agents who devoted all of their time to investigation work for it. All the other professional groups were allotted special agents.

There were times, of course, when a complaint or other matter which required investigation, would be received by two or possibly three professional boards from the same territory at or near the same time. Each Board would dispatch its own agent. Each Board was allotted a given amount of money for law enforcement, by the legislature each biennium and the expense thus incurred was paid out of its funds set aside for it.

The Department believed that some system should be devised that would eliminate this duplication of expense. This was brought about by the creation of the Law Enforcement Bureau within the Department and all agents were merged under the unified control of this bureau. Agents are no longer attached to a particular Board but are now classified as agents of the Department of Public Instruction. The expense incurred by the agents is paid out of the administrative fund.

The state is divided into districts and each inspector assigned a given district in which he makes all investigation regardless of character. The investigations include those for the Board of Pharmacy, Medical Licensure, Dental, Undertakers, Engineers, Accounting, Architects, Optometry, Barbers, etc.

Complaints are sent to the Bureau which distributes them to the agents. Reports of all investigations are sent to the respective Boards and to the bureau. The prosecutions are conducted by the bureau but only when advised by the Board that this is warranted. No action is taken against an individual until after the matter has first been considered by the Board or its enforcement executive.

The Board does not believe that this system is perfect at the present time but believes it is capable of improvement. From an economical standpoint it is based upon sound reasoning.

When first proposed, the Boards administering the laws applying to all Healing Arts, endeavored to have a separate unit to be known as the Medical Arts Unit, allotted for their particular use but were unsuccessful. At the present time, ten agents are employed by the Department and as a part of their time is given to the work of the Board of Pharmacy, it has enabled the Board to increase the scope of its field work.

The work, naturally, has not always been satisfactory. With men untrained in the work, it does not seem reasonable to expect that it would be. During the year in which the system has been in force, there has been distinct improvement. Some agents have, of course, grasped the work more quickly than others and perform more satisfactorily.

The principal criticism which reaches the Board from the drug trade is that the agents are not pharmacists. It is true they are not with one exception, one of the Board's special agents being a pharmacist. I presume that barbers, accountants, engineers, etc., respectively, make complaints of a similar character.

The Pennsylvania Board is interested in this question regarding the employment of pharmacist investigators by the Boards in other states. It does not, of course, have control over the employment of the agents at the present time. One of its finest agents who has been in its employ for almost fifteen years is not a pharmacist.

It is true that in some states the Board of Pharmacy does not enforce the Pharmacy Laws. I understand it does not in the District of Columbia and in many states the services of a detective agency is frequently employed. I believe, too, that there are some members of Boards of Pharmacy who believe the Board should be relieved of that duty. In a survey taken in a southern

state recently, it was recommended that the enforcement should be entrusted to the Department of Agriculture, and that investigations should be made by its agents.

Possibly the most striking example of non-technical supervision which might be cited in support of the employment of non-pharmacist agents is that which is required by the Federal Constitution *viz.*, that the secretary of the Army and Navy be civilians. More recently, should it not be mentioned that at present the entire business structure of the nation, from the largest to the smallest, is under the supervision of an Army General.

In both of these instances the responsible administrator is surrounded with technical advisers. The situation under the Pennsylvania system as it applies to the Law enforcement in which we are interested is quite the reverse, the agent being required to secure the information and forward it to the Board which is composed of technically qualified persons.

In the absence of Mr. Parr, the subject of "Law Enforcement in Michigan" was discussed by Mr. Henry of Michigan.

At this time, the Chairman appointed a nominating committee consisting of R. P. Fischelis, *Chairman*, Mr. Costello and Mr. Heine.

Dr. Fischelis, of New Jersey, spoke upon the "Importance of Synonyms in the Enforcement of Drug Standards and Their Relationship to the Enforcement of Pharmacy Laws." He recommended that the Conference reaffirm their stand on synonyms to the U. S. P. Revision Committee. Upon motion of Mr. Henry, seconded by Mr. Durham, the recommendations of Dr. Fischelis were passed on to the U. S. P. Revision Committee for inclusion in the new revision.

The following resolution was presented to the Conference:

> *Resolved*, That the N. A. B. P. request the Conference of Pharmaceutical Law Enforcement Officials to determine ways and means of providing more adequately for the protection of the public in safeguarding all functions that have to do with prescription service from the time a prescription is written for a patient to the ultimate delivery of the finished medicine, so as to assure a continuity of adequate supervision in this important health function.

It was moved by Dr. Fischelis, seconded by Mr. Schaefer, that the Chairman appoint a Committee to study the resolution and report. The question was discussed by Messrs. Henry, Schaefer, Fischelis and Swain, and adopted.

Chairman Swain next referred to the proposed amendment to the National Foods and Drug Act and Narcotic Legislation; it was discussed by Messrs. Henry, A. H. King and H. Schaefer.

The subject of the "Proper Enforcement of Fair Practice Codes for the Drug Industry under the NRA," was discussed by Messrs. Swain, Schaefer and Heine.

The Nominating Committee at this time made the following report. For *Chairman*, R. L. Swain of Maryland; *Secretary and Treasurer*, M. N. Ford of Ohio; for *Delegate to the House of Delegates*, F. C. A. Schaefer of New York. Upon motion of Mr. King, seconded by Mr. Henry, the report was adopted and the officers declared elected by unanimous vote.

Upon motion, duly seconded, the Conference adjourned.

R. L. SWAIN, *Chairman*. M. N. FORD, *Secretary-Treasurer*.

COMMITTEES OF THE CONFERENCE OF PHARMACEUTICAL LAW ENFORCEMENT OFFICIALS.

Chairman R. L. Swain has appointed the following committees of the Conference of Pharmaceutical Law Enforcement officials: **Finance,** *Chairman*, Frederick C. A. Schaefer, New York; Rowland Jones, South Dakota; Wesley MacChilds, Kansas; S. M. Hankins, Florida; Hugo H. Schaefer, New York; **Committee to accurately define the terms, "patent medicine" and "proprietary medicine:"** *Chairman*, A. L. I. Winne, Virginia; George W. Mather, New York; John M. Woodside, Pennsylvania; M. N. Ford, Ohio; R. P. Fischelis, New Jersey; Robert L. Swain, Maryland.

A LEGISLATIVE REPORT.

Presented by Fayetta H. Philip in the House of Delegates, A. PH. A. as a minority report.[1]

"To A. V. Burdine, *Chairman:*

"In presenting this minority report I am not disagreeing with the majority report of the chairman of the Committee, except to this extent. That the report dealt wholly with the work of those outside of our appointed committee and not of the committee's work, while mine deals with actual work of at least one member of the Committee.

"In the first place my appointment to the Committee was made at the time that I was engaged in securing for the drug stores of the United States an exemption ruling from the Tax Division of the Government. It was the day of the Ground Breaking Ceremony for the Institute of Pharmacy Building in Washington, D. C., that I was shown an article in a *Drug Journal*, which stated that prescriptions which contained certain ingredients would be taxed under the new excise tax laws.

"Even though I was told that it was too late to change the ruling, I said it is never too late to right a wrong, and that as I saw the privileges of my profession, they were beyond the tax laws. Briefly stated the arguments were, that when a physician wrote a prescription, its ingredients could not be divulged to his patient, nor separated out for taxing.

"Fellow druggists, the horrors that stared the profession of pharmacy in the face appalled me. I can conceive of no ruling that would have caused more worry to pharmacists. Within an hour I dispatched a letter to the Department and organized a force to combat the evil. Within three days the danger was past, although it was about three months before the red tape of the Government machinery unwound sufficiently that the druggists were officially notified that there would be no tax on prescriptions.

"The personnel who accompanied me to the offices of the proper Government officials were, W. Bruce Philip, Robert L. Swain, Samuel L. Hilton, Dr. Simmons, E. F. Kelly and C. P. Frailey.

"It was not a simple thing, I assure you, but suffice it to say that in the nick of time our protest was entered and justice was secured.

A. RETAIL DRUG CODE.

"There are several important things concerning the Retail Druggist Code, that it is meet that this gathering of pharmacists should be informed about.

"For three days, in August 1933, a general retailer's code was argued before Administrator Whiteside, in Washington. At the end of the session a Code was written which the proper representative of the respective industries signed. I, as your representative, sat through the session and was conversant with the rules that were given to be followed in drawing up our own Code. I am sorry to report that during much of the time I was the only druggist present. The lack of active participation by druggists in the activities which vitally concern them surprised me.

"There are sixty odd thousand retail druggists in the United States and right now every one of them should be awake to the opportunities and dangers of the situation. Never was it more important for them to be organized and individually awake. Men and women of the profession, this is no mere committee report, this is a stirring appeal to rouse you. You can go around and pat yourselves on the back, because the President of the United States exempted professional pharmacists from the labor provisions of the Code, but that won't get you anywhere except perhaps, in your own estimation.

"The profession of pharmacy is practiced by those who are skilled in the art, and by those who use it as a trade. It does not in any way tear down the profession of pharmacy in admitting that those who practice it work certain hours in a drug store, but it does bruise its sensibilities to have the younger generation of pharmacists rant in public about their rights. On one hand there is the fact that the greater number of pharmacists are clerks, while on the other the smaller number are proprietors. Each is interested in the lives of the citizens of the nation and for long hours and short pay serve behind drug counters, seven days in each week. Can these facts be ignored? Why should they be?

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[1] See Report of Committee on Legislation, page 1047, October JOURNAL.

"No one was in a better position perhaps than I was to present definite statistics as to what had already been done to uphold working hours in pharmacy and I beg leave to show you the background that I worked from. In California in 1910 a very rigid eight-hour law for women was enacted. Physicians and professional women were exempted from its rulings. Trained nurses in hospitals desired to be exempted and presented a test case. Unfortunately a woman pharmacist, Miss Ethel E. Nelson, Merrit Hospital in Oakland, was the person used to try to break the 8-hour law. The case was lost in both the local courts and in the Supreme Court of the United States.

"Nevertheless, women pharmacists in California working in drug stores were being considered by the Labor Commissioner as professional women and not to be under the 8-hour labor law, unless they were working in dispensaries in hospitals. Otherwise they were considered under the 9-hour pharmacy law, which the drug clerks had enacted.

"It is necessary to tell that the 9-hour law made by drug clerks had been broken down in a test case, prosecuted by the Druggists' Association of Southern California in conjunction with the California Pharmaceutical Association, but also I must say that there were places where it would still be applicable. Therefore every class of druggists was active in sponsoring a new law. It was just at this critical stage of affairs that a woman pharmacist who was working over eight hours on the prescription and drug counters of the most ethical prescription drug store in San Francisco was arrested for working over eight hours.

"At a conference with a new Labor Commissioner, he stated that even though his predecessor had considered women pharmacists outside the Eight-Hour Labor Law, still he would not make such a ruling; however, he said that he would hold the case in abeyance until we women pharmacists could be declared under the pharmacy law.

"When the legislature was to convene and acts relative to the Eight-Hour Law were to be introduced, I was chairman of the Legislative Committee of the California Pharmaceutical Association. I rewrote the law, and I went to Sacramento and after five weeks of battle enacted the present pharmacy law, which allows any pharmacist, man or woman, to work 128 hours in any two consecutive weeks, but to work only on thirteen days in such two weeks, etc.

"It was some ten or twelve years ago that the California law was enacted, and after organized union labor had fought the passage of the bill every step of the way. Thereafter, at each session of the legislature they tried to include women pharmacists in a general labor law. Finally the Attorney General made a very definite ruling upon the subject. I will couch it only in layman's words, which were to the effect that when the Legislature, through its two respective bodies of representatives, enacted a law regarding women pharmacists, they intended and did classify them as professional and that a general law would not affect them. The written ruling is a treasured possession of the Women—the Women's Pharmaceutical Association of the Pacific Coast.

"Recently, at the Code hearings, when the drug clerks of New York, Baltimore, and other places said such disparaging things about pharmacy, as a profession I defended it by presenting the wording of the California law, which law has been acceptable and workable to both the professional and commercial interests. In its enforcement pharmacy and pharmacists were adjudged professional by the highest of law authorities in California."

THE WORLD'S FAIR AT CHICAGO IN 1934.

Tile and Till for March has an interesting story of Pharmacy's part at the Century of Progress and its management, ably carried on under the direction of Chairman H. C. Christensen, Secretary Frank B. Kirby and Miss Esther Barney, who had charge of the exhibit. Pharmacy's exhibit will be continued with the reopening of the Fair, on June 1st, introducing a new color scheme, greatly enlarged and varied new lighting effects and important rearrangement of the grounds to make room for new buildings and exhibits.

Alf. W. Pauley was a speaker at the mass meeting of Chicago drugdom on March 20th. George L. Secord presided over the sessions.

ASSOCIATION BUSINESS

AD INTERIM BUSINESS OF THE COUNCIL OF THE AMERICAN PHARMACEUTICAL ASSOCIATION, 1933–1934.

Office of the Secretary, 2215 Constitution Ave., Washington, D. C.

LETTER NO. 8.

March 3, 1934.

To the Members of the Council:

45. Use of Text of N. F. V. Motion No. 11 (Council Letter No. 6, page 158) has been carried and P. Blackiston Son & Co., Inc., have been advised.

46. Buckram Binding for N. F. VI. Motion No. 12 (Council Letter No. 6) has been carried and the note executed as directed.

47. Election of Members. Motion No. 13 (Council Letter No. 6, page 160) has been carried and applicants numbered 75 to 131, inclusive, are declared elected.

48. Time of the 1934 Meeting. Motion No. 14 (Council Letter No. 7, page 160) has been carried unanimously and the attached circular was sent to the pharmaceutical press, to the secretaries of state and national associations, to the secretaries of boards of pharmacy, to the deans of schools and colleges of pharmacy and to the officers of the sections and conferences. Arrangements for the meeting and dedication are going forward rapidly.

49. Report of Auditors. The following has been submitted:

February 3, 1934.

Mr. C. W. Holton, Treasurer,
AMERICAN PHARMACEUTICAL ASSOCIATION,
Baltimore, Maryland.

Dear Sir:

I have made an examination of the books and accounts of the AMERICAN PHARMACEUTICAL ASSOCIATION and your report, as Treasurer, for the calendar year 1933, and *I hereby certify* that the total cash and securities on hand at December 31, 1933, amounting to $371,946.44, is correctly stated.

During the year work on the National Headquarters Building in Washington was continued and $234,246.52 was expended from the Headquarters Building fund for this purpose, increasing the cost of real estate owned by the ASSOCIATION to $457,205.46.

All cash receipts have been traced to deposits in banks to the credit of respective funds for which received, and all disbursements have been found evidenced by properly authorized voucher checks.

Balances on deposit with the various banks have been reconciled with Certificates from the Depositories and Investment Securities held by the ASSOCIATION have been examined and found to be in agreement with the accounts shown by your report. These securities, stated in the amount of $140,400.00, are valued at par value as shown by the certificates.

Interest accruing on bonds held by the various funds and trusts has been promptly collected on the due dates and deposited to the credit of the proper account.

During the year 1933, certain U. S. Liberty Bonds held by the ASSOCIATION were called for redemption. An examination and verification was made of all changes resulting from this.

Records maintained by the Secretary of the ASSOCIATION have been examined and transfers of funds from his account to that of the Treasurer have been verified.

Respectfully submitted,

(Signed) W. A. JOHNSON,
Certified Public Accountant.

For the information of the members of the Council and others interested, the following data are quoted from the Treasurer's report for 1933:

JANUARY 1 TO DECEMBER 31, 1933.

BALANCE AND RECEIPTS.

Balance.

Cash in Merchants & Newark Trust Co., Newark, N. J. (including the Apple Fund)		$ 1,773.05	
Cash in Boston Penny Savings Bank		384.21	
Total Balance, January 1, 1933			$ 2,157.26

Receipts.

For the Current Fund:

From the Secretary (see account attached)		$ 25,537.74	
Interest on Deposit, Boston Penny Savings Bank		11.41	
Interest on Deposit, Merchants & Newark Trust Co.		5.79	
Interest on Headquarters Building Fund		5,071.91	
Interest on Life Membership Fund		6,578.33	
Total Receipts for the Current Fund		$ 37,205.18	

For the Permanent Funds:

Endowment	$ 576.71		
Endowment—Sale of Bonds	2,032.88		
Centennial	188.49		
Ebert Legacy	325.00		
Ebert Prize	42.50		
Life Membership	1,817.52		
Life Membership—Sale of Bonds	11,143.63		
Endowed Membership	7.25		
Research	2,649.16		
Research—Sale of Bonds	6,098.63		
Headquarters Building	5,844.82		
Headquarters Building—Sale of Bonds and Note	301,078.36		
Total Receipts for the Permanent Funds		$331,804.95	

For the Trust Funds:

Wm. Procter, Jr. Monument	$ 628.37		
Wm. Procter, Jr. Monument—Sale of Bond	101.43		
J. P. Remington Honor Medal	49.25		
Total Receipts for the Trust Funds		$ 779.05	
Receipts from Operations		$ 49,334.25	
Receipts from Sale of Bonds and Note		320,454.93	
Total Receipts			$369,789.18
Total Balance and Receipts			$371,946.44

DISBURSEMENTS AND BALANCE.

From the Current Fund,
General Expenses:

	Budget Appropriations.	Budget Disbursements.
Salaries	$ 10,800.00	$ 10,383.26
Rent	900.00	935.00
Telegraph and Telephone	200.00	210.67
Clerical Expenses	1,400.00	1,362.67
Printing, Postage and Stationery	1,100.00	814.57
Office Supplies	150.00	199.71
Traveling Expenses	700.00	169.21
Premium on Bonds	50.00	50.00
Auditing	75.00	75.00
Certificates	50.00	11.00
Miscellaneous Expenses	100.00	36.33
Scientific Section	25.00	27.41
Section on Education and Legislation	25.00	23.03
Section on Practical Pharmacy and Dispensing	25.00	13.65
Section on Commercial Interests	25.00	10.10
Section on Historical Pharmacy	25.00	30.97
Commission on Proprietary Medicines	25.00	
Committee on Local Branches	25.00	
Committee on Membership	500.00	281.00
Committee on State and National Legislation	50.00	
Committee on Syllabus	50.00	
Committee on Unofficial Standards	50.00	50.00
Committee on Pharmacy Week	250.00	250.00
Inter-Society Color Council	25.00	25.00
International Pharmaceutical Federation	120.00	
Metric Association	10.00	
American Conference on Hospital Service	25.00	25.00
Headquarters Building Campaign	1,000.00	814.32
Year Book	3,750.00	3,409.08
Library	50.00	
	$ 21,580.00	$ 19,206.98
Open Accounts:		
JOURNAL	$ 11,000.00	$ 9,504.72
National Formulary	1,800.00	4,231.01
Recipe Book	500.00	130.51
Badges and Bars	50.00	
Total Budget Appropriations	$ 34,930.00	
Total Budget Disbursements		$ 33,073.22
Federal Tax on Checks		4.50
		$ 33,077.72
From the Permanent Funds:		
Endowment Fund, Purchase of Bonds	$ 2,050.03	
Ebert Prize, Medal for 1933	49.20	
Life Membership, Transfer of Interest and Tax	6,578.37	
Life Membership, Purchase of Bonds	6,150.01	
Research, Purchase of Bonds and Tax	6,150.03	
Research, Awards for 1933–1934 and Tax	1,000.02	
Research, National Conference on Pharmaceutical Research and Tax	25.02	

Research, Expenses for Reprints, etc., and Tax	18.86	
Headquarters Building, Transfer of Interest	5,071.91	
Headquarters Building, Architect's Fees and Expenses	6,950.56	
Headquarters Building, Payment of Note and Interest	30,005.84	
Headquarters Building, Interest on Mortgage	2,002.00	
Headquarters Building, Taxes	694.32	
Headquarters Building, Payment on Building	227,583.73	
Total Disbursements from Permanent Funds by Voucher Checks and Charges		$294,329.90
From the Trust Funds:		
Remington Honor Medal, Medal for 1933	$ 35.45	
Total Disbursements from Trust Funds by Voucher Checks		35.45
		$327,443.07
Credits to Permanent and Trust Funds of Excess of Receipts and Disbursements		38,218.65
Total Disbursements		$365,661.72
Balance in Current Fund:		
Cash in Merchants and Newark Trust Co. (including Apple Fund)	$ 3,840.84	
Cash in Boston Penny Savings Bank	395.62	
Cash in Baltimore Trust Co., Secretary's Account	2,048.26	
Total Balance in Current Fund, December 31, 1933		$ 6,284.72
Total Disbursements and Balance		$371,946.44

COMPARISON OF FUNDS.

Current Fund:	Dec. 30, 1932.	Dec. 30, 1933.
Cash in Merchants and Newark Trust Co.	$ 1,773.05	$ 3,840.84
Cash in Boston Penny Savings Bank	384.21	395.62
Cash in Baltimore Trust Co.		2,048.26
	$ 2,157.26	$ 6,284.72
Permanent Funds:		
Endowment Fund	$14,631.09	$ 15,190.65
Centennial Fund	5,552.45	5,740.94
Ebert Legacy Fund	7,954.82	8,279.82
Ebert Prize Fund	1,051.60	1,044.90
Life Membership Fund	41,209.81	36,442.58
Endowed Membership Fund	125.00	132.25
Research Fund	62,932.58	64,486.44
Headquarters Building Fund	500,591.00	494,252.34
Total Permanent Funds	$634,048.35	$625,569.92
Trust Funds:		
Wm. Procter, Jr. Monument Fund	$ 16,646.72	$ 17,276.52
Jos. P. Remington Honor Medal Fund	1,289.79	1,303.59
Total Trust Funds	$ 17,936.51	$ 18,580.11
Summary of Funds:		
Current Fund	$ 2,157.26	$ 6,284.72

Permanent Fund	634,048.35	625,569.92
Trust Funds	17,936.51	18,580.11
Total Funds	$654,142.12	$650,434.75

SUMMARY OF ASSETS AND TRUST FUNDS.

	Dec. 31, 1930.	Dec. 30, 1931.	Dec. 30, 1932.	Dec. 30, 1933.
Current Funds	$ 4,478.44	$ 2,691.32	$ 2,157.26	$ 6,284.72
Permanent Funds	621,347.10	632,606.81	634,048.35	625,569.92
Total Assets	$625,825.54	$635,298.13	$636,205.61	$631,854.64
Trust Funds	16,769.71	17,357.52	17,936.51	18,580.11
	$642,595.25	$652,655.65	$654,142.12	$650,434.75

50. St. John's University, College of Pharmacy, Student Branch, A. Ph. A. The following application has been submitted with the dues of the applicants:

"We, the undersigned students in the course of Pharmacy of St. John's University, College of Pharmacy, desire to establish a student branch of the AMERICAN PHARMACEUTICAL ASSOCIATION at the University and hereby petition the Council of the AMERICAN PHARMACEUTICAL ASSOCIATION to approve the formation of the Branch and its preambles and by-laws as submitted herewith.

Andor Hacker
Herman J. Steinberg
Ada J. Bizzarri
Seymour Stern
Libera Palmeri
Robert Timmel
Bernard Meyerson
William McKaba
Alexander Becker
Harry Figatner
Max Vogel
Irving Koenig
William Matz
Nicholas Arancio
Nicholas Caridi
Patrick J. Dishkin
Arthur De Ianni
Jack Ziving
Herbert Bernstein
Armando Font
Henry Wishinsky.

CONSTITUTION.

"*PREAMBLE.*—This Branch has been established to stimulate a greater professional and scientific interest in the students at St. John's University and to acquaint students with the various pharmaceutical organizations and their work before they go out into practice. We, the undersigned, do hereby resolve to constitute ourselves into a student branch of the AMERICAN PHARMACEUTICAL ASSOCIATION for the purpose of advancing the objects for which the body was founded. The Branch hereby adopts for its guidance the Constitution and By-Laws of the AMERICAN PHARMACEUTICAL ASSOCIATION, and its members hereby subscribe to them."

The By-Laws follow those of the University of Wisconsin Student Branch, printed on page 76, *et seq*, January JOURNAL, 1932, this obviates the necessity of reprinting.

(*Motion No. 15*) *It is moved by Kelly that the application for the formation of the St. John's University, College of Pharmacy, Student Branch and the proposed Constitution and By-Laws be approved.* A vote is called for at this time but will be considered as tentative if there is objection or if any member wishes to discuss it.

51. Applicants for Membership. The following applications properly endorsed and accompanied by the first year's dues have been received:

No. 132, Samuel H. Shagaloff, 263 Frankel Blvd., Merrick, N. Y.; No. 133, Jack Arden Keyes Lemon, c/o Drug Trading Co., Toronto, Canada; No. 134, Cyril E. Souch, c/o Jury & Lovell Ltd., King St. E., Oshawa, Canada; No. 135, Benjamin Davidov, 5300 Edmondson Ave.,

Baltimore, Md.; No. 136, F. E. Johnston, President Shuptrine Co., 31 Barnard St., Savannah, Ga.; No. 137, Harry Vane, Dover, Delaware; No. 138, Emil G. Reichlin, 72 Davis Ave., Kearny, N. J.; No. 139, George P. Grau, Conkling St. & Fait Ave., Baltimore, Md.; No. 140, George W. Brittingham, Wilmington, Delaware; No. 141, E. W. Sterling, Church Hill, Md.; No. 142, H. L. Chichester, 290 Washington Ave., Macon, Ga.; No. 143, Samuel M. Goodman, 24 Brauford Pl., Newark, N. J.; No. 144, Samuel Solomon, 631 W. Lexington St., Baltimore, Md.; No. 145, Violet B. Noll, 851 N. Bentalou St., Baltimore, Md.; No. 146, Charles Pfeifer, 820 E. 33rd St., Baltimore, Md.; No. 147, George H. Dannettel, 301 S. Broadway, Baltimore, Md.; No. 148, Frank M. Budacz, 3138 O'Donnell St., Baltimore, Md.; No. 149, J. S. Patti, 501 Washington Blvd., Brentwood, Md.; No. 150, Emil P. Martini, 47 Linden St., Hackensack, N. J.; No. 151, J. H. Hoagland, 365 George St., New Brunswick, N. J.; No. 152, George A. DeSesso, Mendham Rd., Gladstone, N. J.; No. 153, Bernard John Preston, Jr., 351 Yale Ave., Baltimore, Md.; No. 154, Theodore Thomas Dittrich, 1300 N. Milton Ave., Baltimore, Md.; No. 155, James Jenkins, Ripley, Tenn.; No. 156, Donald Wheeler Butler, Box 2112 University Sta., Gainesville, Fla.; No. 157, Edmund Donald Boudreau, 15 Center St., Bernardsville, N. J.; No. 158, Alan Norris, 216 Medical Arts Bldg., Hamilton, Ont., Canada; No. 159, Marjorie Barr Moore, Abbott Laboratories, N. Chicago, Ill.; No. 160, Harry Stine, 700 W. 175th St., New York, N. Y.; No. 161, George G. Biddle, 7743 Colfax Ave., Chicago, Ill.; No. 162, Felix H. Kaminski, 808 S. Milton Ave., Baltimore, Md.; No. 163, Marguerite F. Crozat, 4435 Hamilton St., New Orleans, La.; No. 164, Charles Werner, 622 Main St., Tell City, Indiana; No. 165, William A. Worner, 705 Canal St., New Orleans, La.; No. 166, William L. Gruber, 338 S. 19th St., Newark, N. J.; No. 167, Raymond L. Thatcher, 56 Tiona Ave., Bellerville, N. J.; No. 168, Michael Joseph Dausch, 501 N. Glover St., Baltimore, Md.; No. 169, Zeal M. Gibson, 1731 Halyoke Ave., E. Cleveland, Ohio; No. 170, Otto P. Gray, 41st St. & Fulton Ave., Cleveland, Ohio; No. 171, Anthony S. Casabona, 85 Glenridge Ave., Glen Ridge, N. J.; No. 172, Harold Gomes Cassidy, 188 E. McMillan, Cincinnati, Ohio; No. 173, Lillian Richards, Herman Kiefer Hospital, Detroit, Michigan; No. 174, Thomas J. C. Johnson, 5 William Street, Cardigan, South Wales; No. 175, Y. Thomas Oester, Box 100, Notre Dame, Md.; No. 176, William H. de Hartog, 332 Fon du Lac St., Waupun, Wisconsin; No. 177, Ralph A. Clark, N. Broad St., Phillipsburg, N. J.; No. 178, A. Lee Caldwell, 5637 Carrollton Ave., Indianapolis, Ind.; No. 179, Lewis William Butz, Delaware Ave. & Vine St., Philadelphia, Pa.; No. 180, Sylvester H. Dretzka, South Milwaukee, Wisconsin; No. 181, H. D. Barnett, 117 E. Potomac St., Brunswick, Md.; No. 182, T. B. Smith, 101 N. Ashley St., Valdosta, Ga.

(*Motion No. 16*) *Vote on Applications for membership in the American Pharmaceutical Association.*

52. Local Secretary for 1933–1934. The Local Committee on Arrangements for the coming meeting was selected by the District of Columbia Pharmaceutical Association. President Paul Pearson and Secretary A. F. Gorsuch are serving as chairman and secretary, respectively, of the Committee.

The Committee has recommended Mr. F. A. Delgado as local secretary. Mr. Delgado is connected with the Department of Commerce and has been a regular attendant at A. PH. A. meetings.

F. A. Delgado is nominated by Kelly as local secretary. If other members of the Council desire to submit nominations they are requested to do so promptly in order that a vote may be called for promptly.

53. Headquarters for the 1934 Meeting. The local Committee on Arrangements has recommended the Hotel Shoreham as headquarters. The hotel is located on Connecticut Avenue, out of the business district, and has ample accommodations. A special rate of $4 per day per person for single room, and $3 per day per person for double rooms has been arranged, all rooms with combination shower and bath.

(*Motion No. 17*) *It is moved by Kelly that the Hotel Shoreham be approved as headquarters for the 1934 meeting.* A vote on this motion will be called for in about ten days.

E. F. KELLY, *Secretary.*

Eighty-second annual meeting of AMERICAN PHARMACEUTICAL ASSOCIATION and dedication of the American Institute of Pharmacy during week of May 7th. See Transportation under department "Societies and Colleges."

PROCEEDINGS OF THE LOCAL BRANCHES

"All papers presented to the Association and Branches shall become the property of the Association with the understanding that they are not to be published in any other publication prior to their publication in those of the Association, except with the consent of the Council."
—Part of Chapter VI, Article VI of the By-Laws.

ARTICLE III of Chapter VII reads: **"The objects and aims of local branches of this Association shall be the same as set forth in ARTICLE I of the Constitution of this body, *and the acts of local branches shall in no way commit or bind this Association, and can only serve as recommendations to it.* And no local branch shall enact any article of Constitution or By-Law to conflict with the Constitution or By-Laws of this Association."**

ARTICLE IV of Chapter VII reads: **"Each local branch having not less than 50 dues-paid members of the Association, holding not less than six meetings annually with an attendance of not less than 9 members at each meeting, and the proceedings of which shall have been submitted to the JOURNAL for publication, may elect one representative to the House of Delegates."**

Reports of the meeting of the Local Branches shall be mailed to the Editor on the day following the meeting, if possible. Minutes should be typewritten with wide spaces between the lines. Care should be taken to give proper names correctly and manuscript should be signed by the reporter.

CHICAGO.

The monthly meeting of the Chicago Branch of the AMERICAN PHARMACEUTICAL ASSOCIATION was held at the University of Illinois College of Medicine, February 20, 1934.

Dr. Mary Rising, Professor of Chemistry, University of Chicago, was introduced as the speaker of the evening. Her subject was entitled "Hypnotics."

Dr. Rising introduced the subject of hypnotics by beginning with a short history of the changes during the years in the use of simple drugs up to the present-day use of many of the complicated coal-tar products.

The production of procaine, which is far less toxic than cocaine, was cited as a triumph of the synthetic chemists.

Hypnotics were described as drugs which produce sleep, but do not relieve pain. To-day they are taking the place of narcotics to a great extent where only sleep is wanted.

A discussion followed of many of the popular barbiturate derivatives and their structural formula was shown by lantern slides. Mention was made of the possibilities of further research work on the barbiturates and what the chemists are striving for.

After the very interesting presentation by Dr. Rising, Mr. Morrison, head of the drug department of the University of Illinois Research Hospital, exhibited some prescription incompatabilities that he had encountered and suggested methods of overcoming them.

LAWRENCE TEMPLETON, *Secretary.*

NEW YORK.

The February meeting of the New York Branch of the AMERICAN PHARMACEUTICAL ASSOCIATION was held in the College of Pharmacy, Columbia University. President Ballard was in the chair, and about fifty members and their guests attended.

After the meeting had been called to order the report of the secretary was read and accepted.

Due to the absence of Treasurer Currens, his report was read. Dr. Bilhuber, *Chairman* of the Audit Committee, then reported that he had gone over the accounts with the *Treasurer*, and had found everything in order.

Chairman Lehman, of the Committee on Education and Legislation, reported by letter that he had appointed Messrs. Dyer and Dworkin to serve on his Committee.

Chairman Kassner, of the Professional Relations Committee, next reported the appointment of Messrs. Gerstner and Frederick Lascoff as members of his Committee.

Chairman George Simpson, of the Membership Committee, now reported the following appointments to his Committee: Messrs. Raubenheimer, Kidder, Ligorio, Hutchins and Lippe. Applications for Branch membership of the following were reported by Mr. Simpson: Edward Klar, Samuel Henkin, Jonathan Gordon, Ralph Foran and Frank Hitchcock. Mr. Harry Stine's application for membership in the AMERICAN PHARMACEUTICAL ASSOCIATION was also submitted.

Following a motion by Dr. H. V. Arny, seconded by Dr. Kassner, the applications for Branch membership were accepted and the applicants were voted in as members. The application of Harry Stine was forwarded to Secretary Kelly.

Chairman Dauer, of the Committee on the Progress of Pharmacy, reported the appointment of Messrs. Kassner, Schaefer, Dyer, Wimmer and Kern to membership on his Committee.

The president then announced the topic for the March meeting and for the April meeting and urged all present to attend.

Following this President Ballard introduced the speaker for the evening, Mr. Marshall G. Meriam, who discussed the Manufacture of Clinical Thermometers. The speaker was assisted by Mr. Barthen, who demonstrated while Mr. Meriam discussed the various steps in the manufacture of clinical thermometers.

The speaker began his discussion by briefly reviewing the history of the clinical thermometer, and also described some of the early types. He then proceeded with a description of the manufacture of the glass tubing used in making thermometers. Several of his exhibits showed clearly some of the intermediate stages in drawing out the glass. The actual manufacture of a thermometer was then carried out by Mr. Barthen, while Mr. Meriam carefully explained each step. Of unusual interest was the projection on a screen of the constriction in a clinical thermometer. This showed very clearly how the constriction operates. The importance of aging thermometers before calibration was pointed out by the speaker. The final calibrating of the finished thermometer was then described.

Many practical hints for the use and sale of thermometers were included by Mr. Meriam. He carefully demonstrated the proper method for "shaking down," and likewise explained the reasons for the various prices of thermometers.

Many types and forms of clinical thermometers and cases were shown, and Mr. Barthen went through the manufacture of thermometers repeatedly until every one present had seen the delicate operations at close hand.

At the completion of Mr. Meriam's address a rising vote of thanks was accorded the speaker and his assistant, and the meeting was formally adjourned to give every one an opportunity to see the exhibits.

RUDOLF O. HAUCK, *Secretary.*

ANNOUNCEMENT OF APRIL MEETING.

The meeting of New York Branch, A. PH. A., on April 9th will be held at 8:15 P.M. in the College of Pharmacy, Columbia University, 115 W. 68th St., New York City. This meeting will be devoted entirely to a celebration of the 50th Anniversary of the National Formulary. Plans at present call for the cooperation of the Kings County Pharmaceutical Society and the Deutsches Apotheker Verein. Persons prominently connected with the N. F. work will be present and it is hoped to have Dr. Charles F. Schleusner recount some reminiscences.

RUDOLF O. HAUCK, *Secretary.*

NORTHERN NEW JERSEY.

The February 19th meeting of the Northern New Jersey Branch of the AMERICAN PHARMACEUTICAL ASSOCIATION was one of the most interesting that we have had. The regular routine of business was suspended by President Little and the members enjoyed two very good addresses, one by Mr. Charles Nichols, on "Pharmacy in the Near East," and the other by Doctor James C. Munch on the new hormone "Tissue Extract."

Mr. Nichols, the first speaker, was born in the Near East and attended the American University of Beirut where he studied Pharmacy. His introductory remarks were, therefore, devoted to a description of the university and the country surrounding it. He then began the story of the life of a pharmacy student in that English-speaking institution.

In order to matriculate in the course in pharmacy, one must have already earned a B.A. degree or possess its equivalent in education. The work is divided into three parts, first a preliminary academic year preparatory to a year of practical work in a licensed pharmacy, which is followed by another period of class and laboratory instruction.

The student undergoes regular course examinations at the end of the first year. He then sits in special oral examination with a commission from the Turkish Government before he is permitted to engage in the year of practical work. This last inquisition is conducted either in French or Turkish according to the wish of the candidate. The next serious examinations are the finals in his senior year.

Upon graduation the student is presented with the degree of Master of Pharmacy by the

University and a diploma from His Majesty's Imperial Medical Science University. These credentials take the place of a state board certificate and give their holders the right to practice pharmacy in any part of Turkey, Egypt and the Sudan.

"The pharmacist in the Near East," Mr. Nichols said, "is ranked professionally with the physician and works in close harmony with the latter. The pharmacies too, are truly professional, and strange as it may seem French is the language of the prescription."

Doctor Munch, next on the program, began his talk on "Tissue Extract" with a demonstration of the variation taste with different individuals. Mr. Arnold Quici assisted in the experiment. Doctor Munch then explained that Tissue Extract is the name which has been given to a hormone obtained from the pancreas, principally, but also from other tissues and from the urine. It appears that this hormone is elaborated in the pancreas, passes into the circulation, is deposited in various organs (brain stem, liver, kidneys, etc.) and is eventually excreted in the urine. When the pancreas of an experimental animal is removed, there is a prompt decrease in the amount of the hormone in the urine or tissue.

It is obtained in connection with extraction of insulin from pancreas, on a commercial scale. The ground pancreas is extracted with acid alcohol, allowed to stand, neutralized and filtered. The filtrate which contains both insulin and Tissue Extract is then concentrated, the fat removed, and the insulin precipitated out with ammonium sulphate at the isoelectric point. The supernatant solution is concentrated *in vacuo*, insoluble material filtered off and the "Tissue Extract Concentrate" is available for standardization and use. After a series of intravenous injections of epinephrine have been made in a surgically anesthetized dog, a series of injections of Tissue Extract are given and the fall in blood pressure determined. A mixture of known volumes of Tissue Extract and epinephrine is then injected until that proportion is determined which causes neither a rise nor a fall in blood pressure. One unit has been considered to be that volume of Tissue Extract neutralizing the pressor activity of 1 gamma (0.001 mg.) of epinephrine. Material used in research and in clinical studies contains 10 units per cc.

The action of epinephrine has been neutralized in every method by which its action has been measured (blood pressure, blood sugar, constricting tissues, etc.).

Clinically studies on about 500 patients with angina pectoris have shown that the course of treatment produced complete disappearance of the anginoid pains in 50 per cent; disappearance during treatment in an additional 35 per cent, and no demonstrable effects in 15 per cent. In treating about 100 cases of thrombo-angiitis obliterans and endarteritis obliterans, about the same percentage of relief was observed. Tissue Extract appears to be useful in treating vasomotor disturbances such as angina pectoris, Buerger's disease and intermittent claudications.

The addresses concluded, the Membership Committee nominated the following individuals for membership in the branch: Anthony S. Casabona, J. Stanley Steiner and Raymond L. Thatcher. They were elected.

A. P. Shenkel, Division Sales Manager for Sharp and Dohme, spoke for a few minutes, after which the meeting was adjourned.

L. W. RISING, *Secretary.*

PITTSBURGH.

The Pittsburgh Branch of the AMERICAN PHARMACEUTICAL ASSOCIATION met February 27, 1934, in the lecture room of the Falk Clinic. Prof. Clarence T. Van Meter presided.

An election of officers was held. The following will serve the Pittsburgh Branch for the 1934–1935 term:

President, Raymond Hornfeck
Vice-President, John Ray Burrows
Secretary, Frank S. McGinnis
Delegate, C. Leonard O'Connell.

Doctors Leo H. Criep and Ralph V. Robinson, members of the teaching staff of the School of Medicine, University of Pittsburgh, addressed the group. The following is a short abstract of the paper.

"The United States spends on an average of about four hundred million dollars a year on patent medicines. These products are frequently not patented at all, because the manufacturer cannot prove that they are either new or useful. Furthermore, the formula would have to be disclosed, and this would rob the product of the very secrecy upon which the manufacturers depend for success of marketing the nostrum. While the Pure Food and Drugs Act of 1906 was undoubtedly a step in the right direction, the law is sufficiently weak as to allow many loopholes, and permit a great deal of quackery.

"The agitation at the present time on the Tugwell Bill, or a modification thereof, should be supported by the medical and pharmaceutical professions. Steps should be taken in the direction of curbing the unfair and fraudulent advertising going over the air daily. Unless this is done soon, we shall find that its harmful effects will, by far, exceed that of newspaper advertising.

"It is to the credit of high-grade pharmaceutical journals that they have always spoken against the frauds practiced by some patent medicine manufacturers. For a great deal of this the medical profession is to blame, because it has helped to popularize various proprietary medicines. The weakness of the courses of pharmacology and therapeutics in our medical schools to-day is also an important factor.

"A plea was made for closer coöperation between the medical and the pharmaceutical profession."

Dr. Ralph V. Robinson presented "Burke and Hare" in a very entertaining and informative manner. His introductory remarks concerned the history of early medicine, and how schools of anatomy came into being. He told of the life of Burke and Hare, and the part they played in supply material for anatomical study. Interesting lantern shades were used by Dr. Robinson, for illustrating the escapades of the notorious characters, "Burke and Hare."

FRANK S. MCGINNIS, *Reporter.*

ST. JOHN'S UNIVERSITY, COLLEGE OF PHARMACY, STUDENT BRANCH.

Thirty students, several Alumni and members of the faculty attended a dinner in Brooklyn in honor of the institution of the St. John's University, College of Pharmacy, Student Branch of the A. PH. A. Permission had been granted to proceed with the dinner pending the parent association. Max Vogel, '34, president of the newly organized branch acted as toastmaster; the speakers were Professor John J. Corcoran and Dr. Otto Raubenheimer; other guests included Professor Vernon Brooks and Professor Frank Bulda.

In his most enlightening and inspiring talk Dr. Raubenheimer, the guest of honor, traced the history of the AMERICAN PHARMACEUTICAL ASSOCIATION and explained the work carried on by the organization. He described the development of an American literature of pharmacy, specifically discussing the PROCEEDINGS, the YEAR BOOK, the JOURNAL, the National Formulary and the Recipe Book published by the ASSOCIATION. The value of the work done by the Scientific Section, the Historical Section and the Section on Dispensing Pharmacy was also discussed by Dr. Raubenheimer.

Other officers of the newly formed branch are: Herman J. Steinberg, '34, *Vice-President;* Bernard Meyerson, *Secretary;* and William McKaba, '34, *Treasurer.*

FIFTIETH ANNIVERSARY, TEMPLE UNIVERSITY.

Temple University celebrated its fiftieth anniversary the week of February eleventh, with many meetings and activities suitable to the occasion. The college, founded by Russell H. Conwell, author of the famous lecture "Acres of Diamonds," has grown in student enrollment from seven in 1884 to approximately twelve thousand in 1934. The property and equipment accumulated during this period is valued at about eight million dollars.

The School of Pharmacy promoted an elaborate program which included displays, demonstrations, visitations and meetings of interest to pharmacists, physicians and dentists. The Dean and Faculty entertained at dinner the delegates in attendance from other Schools of Pharmacy, State Boards and Pharmaceutical and Drug Associations. United States Senator Royal S. Copeland delivered the principal address at this meeting, and at the Founder's Day graduation exercises he was the recipient of the honorary degree of Doctor of Science.

Short speeches of congratulation and felicitation were made by J. W. Sturmer, Dean, Phila. College of Pharmacy, representing the American Association of Colleges of Pharmacy; R. E. Lee Williamson, secretary, Federal Wholesale Druggists' Association; John M. Woodside, member, Penna. State Board of Pharmacy; Robert P. Fischelis, president-elect, AMERICAN PHARMACEUTICAL ASSOCIATION; W. Bruce Philip, general counsel, N. A. R. D.; W. Scott Taylor, Jr., president, New Jersey State Board of Pharmacy; Wilmer Krusen, president, Philadelphia College of Pharmacy; Leo G. Penn, president, Philadelphia Association of Retail Druggists; John C. Walton, Executive Committee, Penna. Pharmaceutical Association; Frank H. Eby, president, Phila. Branch, AMERICAN PHARMACEUTICAL ASSOCIATION; Charles H. LaWall, dean, Philadelphia College of Phar-

macy; Lloyd N. Richardson, president, Maryland Board of Pharmacy; John C. Krantz, Jr., second vice-president; Henry Brown, Executive Committee, Penna. Pharmaceutical Association; Charles T. Pickett, secretary, Philadelphia Association Retail Druggists.

Robert P. Fischelis, president-elect of the AMERICAN PHARMACEUTICAL ASSOCIATION, made the principal talk at the Pharmacy convocation Wednesday afternoon.

A large number of guests, students and alumni listened to his scholarly paper "Pharmacy in Our Changing Era." Parts of the address follow:

PHARMACY IN OUR CHANGING ERA.
BY ROBERT P. FISCHELIS.

"You must know the changing needs of humanity if you would succeed in life. In business, in your profession, in your housekeeping, whatever your life, that one thing is the secret of success. You must first know the demand. You must first know what people need, and then invest yourself where you are most needed." Thus spoke Russell Conwell, the founder of this great University, in his oft-repeated lecture, "Acres of Diamonds."...

At this convocation, commemorating as it does the fiftieth anniversary of the beginning of Temple University, and the thirty-third anniversary of the organization of its School of Pharmacy, it may profit us to spend a few minutes in contemplating the Conwell success formula as it applies to the field of endeavor in which we are engaged....

How careful have we been to examine the changing needs of humanity with respect to pharmacy? Have we honestly and intelligently endeavored to ascertain what, among the things we have to offer, the people really need? Have we endeavored to invest ourselves where we are most needed? The answers to these questions will reveal how closely we have approached the standards of success as visualized by the founder of this University....

We know that the demand for the type of pharmaceutical service which engaged the major part of the retail druggist's attention is no longer demanded to the extent that it was when Temple University organized its School of Pharmacy in 1901.

Prescription work has not increased. New and more complicated products have replaced the simple drugs in the physician's armamentarium. The manufacturing function has been almost entirely eliminated from many of our retail drug stores. This is partly due to the necessity for proper chemical and biological control of manufacturing processes or of finished products, which cannot be carried out in the ordinary drug store laboratory. It is also partly due to the prohibition era, during which it was made difficult and in some instances impossible for pharmacists to obtain alcohol for manufacturing purposes without endless record-keeping and official red tape. Nor was it possible to compete with large-scale producers who were able to obtain specially denatured alcohol in quantities at greatly reduced prices, free from the revenue tax. It was also partly due to the growing apathy on the part of pharmacists toward professional work, and their avidity for any kind of merchandising activity which would help to keep their establishments going at a profit.

During this same period "big business" entered the field of medicine. Pharmaceutical manufacturing establishments of long standing became the playthings of financiers. Advantage was taken of the fact that anybody can enter the medicine manufacturing business in all states of this Union without meeting any requirements as to scientific or professional training or moral character. Our inadequate food and drug laws made it possible for individuals and corporations to grow wealthy at the expense of citizens who take it for granted that whatever anyone may print or say over the radio about a medicine is true. Patent and proprietary medicines whose formulas are unrevealed were forced in constantly increasing numbers upon the pharmacist's shelves by the creation of a public demand through advertising of one kind or another and by high-pressure sales methods. Manufacturers of these products set themselves up as authorities on the diagnosis and treatment of nearly all ailments to which the human flesh is heir, and with the increasing costs of properly regulated, scientific medical care, they found a fertile field among those who considered the taking of medicine an economical way to health, in the full faith that their Government would permit no fraud in a field of such great importance to the public welfare. Without question, these interests have made inroads upon the practice of medicine and pharmacy, with doubtful benefit at best, and, in many cases, with considerable detriment to the public health.

"Big business" also entered the retail drug

field. It emphasized the merchandising possibilities of every commodity and every service ever offered in retail drug stores. Many pharmacists, seeing the material success that attended the efforts of these organizations, deemed it expedient and wise to follow the lead of the corporation stores. In many instances this left the pharmacist of the old school far behind in the procession toward business success, wondering how long he might be expected to survive, but doing virtually nothing to determine whether the new developments were really filling a public need or whether they were merely a form of exploitation of a gullible and long-suffering public. . . .

How many pharmacists are competent to pass upon the conflicting "scientific" claims of the many hundred so-called antiseptics, cosmetics, patent medicines and sundries which are offered an unsuspecting public as health aids with little or no scientific or even practical background? Here indeed we have a public need which the properly educated pharmacist can fill with profit to himself as well to his clientele. . . . The people want to know the truth about drugs. They obtain exaggerated versions from certain popular literature but these versions are at least as truthful as the advertising which has placed the products criticized among the best sellers of the offerings of the drug store and they have the advantage of warning the public to be on its guard against possible and probable fraud. With increasing doubt of the value of drugs engendered in the public mind, the people will listen to and honor a pharmacist who has the courage to tell the truth, based upon knowledge and facts.

Ali Hafed—in the Conwell lecture "Acres of Diamonds"—traveled thousands of miles from his home in search of diamonds. He died in poverty, but the man who bought Ali Hafed's original farm soon discovered the most perfect diamonds in the garden of the home which Ali had left to wander afar in his ill-fated search. How true of Pharmacy! We wandered far afield in search of material success, and we have left uncovered the acres of diamonds lying in our back yard because we seem to be unable to apply the training and knowledge we have gained at great expense of time and effort to the simple task of finding the human need which we are able to fill.

But, you say, even if we should coöperate more intimately with the medical and dental professions and become an acknowledged source of critical information on the efficiency and value of drug products, would this not lessen rather than increase our income? Certainly we could not be expected to continue to sell the articles which science condemns.

It is true that a fairly general acceptance of a program of this kind would curtail the sale of many products, but it would correspondingly increase the sale of those which are marketed purely on a basis of merit. Pharmacists would no longer hesitate to express their convictions on health matters, and they would rise in public esteem to the level of a true health profession. The utilization of the professional services of pharmacists to their fullest extent would fill a public need for which the public will pay and do so willingly and handsomely.

We have tried many schemes to improve our condition. Practically all of them have failed. Is it not worth trying something which is based upon the fundamental reason for the existence of a profession of pharmacy?. .

If we are to have a strong, militant and effective profession of pharmacy in the future, we must have strong, efficient and forward-looking colleges of pharmacy. We do not need as many as we have, and in the years immediately ahead we shall, no doubt, see a merging of some institutions with others and a complete cessation of activity in a number of these schools. It is important in a transition period such as we are now going through that the profession keep a close check on the type of instruction offered in our colleges. There is an unfortunate tendency in some universities to turn over the direction of schools of pharmacy to administrators who have no pharmaceutical background. It is a mistake for any profession to entrust the destiny of the institutions which train its future personnel to administrators who have not themselves come up through the ranks of the profession. Occasionally an able administrator will be found who, though not a pharmacist, can acquire a sufficient pharmaceutical background over a period of years to enable him to do a fairly good job in promoting pharmaceutical education. In general, however, pharmacy schools which lack the administrative direction of a trained pharmacist do not turn out the best type of raw material needed for the up-building of the profession.

President Beury is to be congratulated upon

having followed the Conwell formula of looking for the diamonds in your own home ground, when selecting as the Dean of your Pharmacy School, to succeed the late Dean Minehart, a man who not only knows pharmacy from actual contact, but whose services to the University over a long period of years have qualified him most admirably to lead this institution to newer and greater spheres of usefulness. Dean Kendig's approach to the problem of educating pharmacists to meet the newer and broader responsibilities of the future has been both statesmanlike and practical. I am glad to pay this tribute to the splendid efforts he is putting forth in your behalf.

We have been spending much time in building up a national pharmaceutical curriculum based upon minimum hours, required subjects and a cultural background. The modern idea of university education is to lay less emphasis upon class work, schedules and required attendance. In the words of Woodrow Wilson, "The University spirit is intolerant of all things that put the human mind under restraint. It is intolerant of everything that seeks to retard the advancement of ideas, the acceptance of truth, the purification of life." We still have a considerable road to travel to place pharmaceutical education on the level of the newer ideas for developing a liberal educational program. The time is not far distant, however, when such a program must be given more serious consideration. Graduate work in our colleges of pharmacy must be developed if we are to man state and national pharmaceutical associations, colleges of pharmacy and boards of pharmacy with the kind of personnel that will develop our profession along lines of greater usefulness.

Finally, it is incumbent upon those who have the management of our two great national associations in charge to give consideration to the possibility of merging their activities. It is not necessary to merge the physical equipment and other assets of these associations in order to bring about a more coördinated program of activity. There should, however, be a clearly defined line of activity which each of our national organizations should undertake, and in which each of them should be considered the acknowledged leader. Both organizations should place their entire resources back of the joint programs and should unselfishly assist each other in carrying their respective programs to a successful issue. This is no time for petty quarrels. There are too many big things at stake. There is within the membership of these national organizations sufficient intelligence and ability to work out an effective plan of coöperation, and such a plan should be worked out without delay.

Allowing to-morrow to take care of itself is, in the long run, a destructive procedure. We are suffering to-day from the lack of foresight and constructive planning of the generation immediately preceding ours. Let us not fall into the same error. Let us also in the spirit of Russell Conwell, remember that Pharmacy is not a thing conceived to please pharmacists. It is a thing with which pharmacists must please mankind in general.

Left, C. Lewis Diehl; *right*, William S. Thompson, Washington, D. C., president, A. PH. A., 1884 (see page 83, February) on Mississippi steamer, St. Louis, 1901. See historical paper by John E. Kramer in this issue of the JOURNAL.

NOTICE TO RESEARCH WORKERS IN PHARMACY.

The Annual Census of Pharmaceutical Research under the auspices of the National Conference on Pharmaceutical Research is being compiled. All reports must be sent promptly to Dr. James C. Munch, 40 North Maple Avenue, Lansdowne, Pa., in order to be included in this year's census. Census blanks may be obtained by writing the office of the *Secretary*, 2411 North Charles Street, Baltimore, Maryland.

EDITORIAL NOTES

DONATION OF MORTARS.

Dr. F. B. Tipton, of Washington, has donated two mortars and pestles, one a lignum vitæ and the other of bell metal which has an interesting recorded history. It was brought to this country from England by Captain Dr. William Stone, November 22, 1633, who landed in Maryland, March 25, 1634. He obtained the mortar and pestle from his father in 1622. The former was Governor of Maryland from August 6, 1648 to July 20, 1654. The history is complete up to the present day—Dr. Tipton received the mortar from Robert Pinkney Stone on March 16, 1931, and it was donated to the AMERICAN PHARMACEUTICAL ASSOCIATION by the former on March 16, 1934.

A COÖPERATIVE MOVE.

The regularly licensed and registered practitioners of Medicine, Dentistry and Pharmacy of Kansas have formed an organization to bring about professional coöperation and enhance the well-being of the public. It is known as "The Public Health Council of Kansas."

LANDMARKS SOCIETY OF ALEXANDRIA TO RESTORE THE STABLER PHARMACY.

A charter for a non-stock corporation has been applied for under the new name of Landmarks Society. It was also voted unanimously to restore the building, as far as possible, to the condition of 1792, using the material recently discovered in the attic of the old Stabler store for this purpose. From the opinions of the architects that have been consulted this restoration of the 1792 conditions appears to be well endorsed. It seems certain, however, that it cannot be completed in time for exhibition in May. The Leadbeater (Stabler) Apothecary was recently acquired for the AMERICAN PHARMACEUTICAL ASSOCIATION.

PERSONAL AND NEWS ITEMS.

Under direction of Chairman **Anton Hogstad, Jr.**, of the Pharmacy Week Committee, Oklahoma Pharmaceutical Association will have an exhibit of a Modern Pharmacy, patterned after that held by Wisconsin Pharmaceutical Association.

Dr. Henry S. Johnson, of Connecticut College, College of Pharmacy, is giving a series of lectures on pharmacy and pharmaceutical preparations to the students in Yale University, School of Medicine, in connection with their course in pharmacology. These lectures are being given at the invitation of Dr. Henry G. Barbour, Head of the Department of Pharmacology in the School of Medicine. Dr. Johnson is being assisted in his work by Prof. Fuller and Mr. Fenney of the Pharmacy Department of the Connecticut College of Pharmacy.

Dr. Edward Kremers delivered the principal address at the celebration of the 50th anniversary of the founding of the School of Pharmacy, Purdue University. The subject of his address was "Pharmaceuticals in the United States as Influenced by the Universities of the Old Northwest Territory."

Secretary **J. Lester Hayman** advises that the campaign in West Virginia has resulted in an increase of 33 1/3% of membership of the State association.

Dr. Paul N. Leech, director of the American Medical Association Laboratories in Chicago, delivered two lectures before Purdue University section of the American Chemical Society. In his first lecture Dr. Leech discussed cosmetics, antiseptics, and proposed food and drug legislation (Copeland bill). He stated that the American Medical Association indorses the intention of the Copeland bill, but that he personally felt it would be better to amend the old bill than to introduce an entirely new one, inasmuch as the old Act has been tested by numerous Supreme Court decisions.

In his second lecture Dr. Leech discussed late developments in the drug field.

Prof. Heber W. Younken recently was expert witness in a case involving the responsibility for two deaths. The determination was based on his testimony following microscopical examination of adhering particles to the bullets that caused the deaths.

On February 28th, the Board of Trustees of The Tennessee Academy of Science unanimously elected **Dr. A. Richard Bliss, Jr.,** director of The Reelfoot Lake Biological Station at Reelfoot Lake, Tennessee.

SOCIETIES AND COLLEGES.

TRANSPORTATION TO THE WASHINGTON MEETING WEEK OF MAY 7TH.

Chairman Theodore J. Bradley of the Transportation Committee and E. F. Kelly, secretary of the AMERICAN PHARMACEUTICAL ASSOCIATION, have been advised by the various passenger associations that the identification ticket plan concession of $1^1/_3$ fare for the round trip has been allowed. Identification certificates will be sent out later to members and those contemplating the trip should see their passenger agents as promptly as possible so that there will be no question when purchase of tickets is made. The tickets are good *via* the same route in both directions and will be sold from April 28th to May 9th, inclusive, and before being honored for return; return portions of the tickets must be validated at Washington or Baltimore. The tickets include thirty days in addition to date of sale and validated tickets will be good for return, leaving on any day within final limit.

Round trip tickets will also be sold on the $1^1/_3$ fare basis going *via* any authorized route published in one-way tariffs returning *via* any other authorized route published in one-way tariffs.

It will be necessary for members when purchasing round trip tickets to present and surrender the identification ticket issued account of the meeting and to indicate to ticket agents which ticket is desired, namely, (1) $1^1/_3$ fare for round trip good for same route in both directions; final return limit thirty days in addition to date of sale. (2) $1^1/_3$ fare for round trip going *via* any authorized route and returning *via* another authorized route. In both cases the final return limit is thirty days in addition to date of sale.

The identification certificates will bear the signature of E. F. Kelly, secretary of the A. PH. A., and will be mailed to members very soon.

PAPERS FOR THE SECTIONS AND CONFERENCES.

Members who will present papers at the Washington meeting of the AMERICAN PHARMACEUTICAL ASSOCIATION should send them in promptly to the Section officers, carbon copies may be sent to the Editor of the JOURNAL A. PH. A., 2215 Constitution Ave., Washington, D. C.

The Scientific Section has issued the following call:

Members and Friends of the Scientific Section, American Pharmaceutical Association:

The 82nd annual meeting will be held in Washington, D. C., during the week of May 7th and will include the dedication of the new headquarters building. The Scientific Section plans to hold several interesting sessions but in order to accomplish this the officers must have your coöperation.

Since the Convention date is much earlier than usual and now is only about six weeks away, it will be necessary for authors of papers to submit titles and very short abstracts to the Secretary by April 15th at the very latest in order that the titles may appear in the printed program. Authors should indicate whether the papers are to be presented in person or by title and should bear in mind that ten minutes is the time limit for the presentation of a paper.

F. E. BIBBINS, *Chairman*, Scientific Section.

L. E. ROWE, *Sec'y*, Scientific Section, c/o Parke, Davis & Co., Detroit, Michigan.

The Scientific Section has received the following papers:

1. "The Effect of Hydrogen Peroxide and Some Oxygenated Terpenes upon Ascaris Lumbricoides," L. W. Butz and W. A. LaLande, Jr.

2. "A New Method for Determining Acetyl Salicylic Acid in the Presence of Other Medicinal Products," R. M. Hitchens.

3. "The Stabilization of Syrup of Ferrous Iodide, U. S. P. X," William J. Husa and Lyell J. Klotz.

4. "Drug Extraction. I. A Study of Various Manstrua from the Standpoint of Swelling Effects, Penetration and Extraction," William J. Husa and Louis Magid.

5. "Drug Extraction. II. The Effect of Fineness of Powder and of Variation in Solvents on the Percolation of Belladonna Root," William J. Husa and C. L. Huyck.

6. "Drug Extraction. III. The Function of Preliminary Maceration in Relation to the Percolation of Belladonna Root," William J. Husa and S. B. Yates.

7. "Drug Extraction. IV. The Effect of Variation in Solvents on the Extraction of Jalap," William J. Husa and Faul Fehder.

SECTION OFFICERS.

Scientific Section.—*Chairman*, F. E. Bibbins, 5840 Washington Blvd., Indianapolis, Ind.; *First Vice-Chairman*, E. V. Lynn, Seattle, Wash.; *Second Vice-Chairman*, H. M. Burlage, Chapel Hill, N. C.; *Secretary*, L. W. Rowe, % Parke, Davis & Co., Detroit, Mich.; *Delegate to the House of Delegates*, W. J. Husa, Gainesville, Fla.

Section on Education and Legislation.—*Chairman*, George C. Schicks, Montclair, N. J.; *Vice-Chairman*, Oscar E. Russell, Elkhart, Ind.; *Secretary*, C. W. Ballard, Mount Vernon, N. Y.; *Delegate to House of Delegates*, W. H. Rivard, Providence, R. I.

Section on Practical Pharmacy and Dispensing.—*Chairman*, M. J. Andrews, University of Maryland, Lombard and Greene Sts., Baltimore, Md.; *Vice-Chairman*, Ralph W. Clark, University of Wisconsin, Madison, Wis.; *Secretary*, R. E. Terry, School of Pharmacy, University of Illinois, 701 S. Wood St., Chicago, Ill.; *Delegate to the House of Delegates*, L. W. Rising, Newark, N. J.

Section on Commercial Interests.—*Chairman*, John A. J. Funk, Galveston, Ind.; *Vice-Chairman*, Henry Brown, Scranton, Pa.; *Secretary*, Robert W. Rodman, 55 Park Ave., Bloomfield, N. J.; *Delegate to the House of Delegates*, R. B. Rothrock, Evansville, Ind.

Section of Historical Pharmacy.—*Chairman*, Louis Gershenfeld, 281 S. 63rd St., Philadelphia, Pa.; *Secretary*, C. O. Lee, Purdue University, Lafayette, Ind.; *Delegate to the House of Delegates*, J. T. Lloyd, Cincinnati, Ohio; *Historian*, E. G. Eberle, 2215 Constitution Ave., Washington, D. C.

CONFERENCES.

National Conference on Pharmaceutical Research.—*Chairman*, E. N. Gathercoal, Chicago; *Vice-Chairman*, William J. Husa, Gainesville, Fla.; *Secretary*, John C. Krantz, Jr., Baltimore; *Treasurer*, Fitzgerald Dunning, Baltimore; *Executive Committee*, H. V. Arny, Montclair, N. J.; R. L. Swain, Baltimore; F. C. Bibbins, Indianapolis.

Conference Pharmaceutical Association Secretaries.—*President*, Robert C. Wilson, University of Georgia, Athens, Ga.; *First Vice-President*, F. B. McCullough, New Albany, Ind.; *Second Vice-President*, E. R. Weaver, Stillwater, Okla.; *Secretary-Treasurer*, Carl G. A. Harring, 20 Glen Road, Newton Center, Mass.; *Delegate to the House of Delegates*, Wm. B. Day, Chicago, Ill.; *Members of the Executive Committee*, J. Lester Hayman, Morgantown, W. Va.; J. J. Gill, Providence, R. I.; Roy Reese, Topeka, Kans.; W. E. Bingham, Tuscaloosa, Ala.

Conference of Pharmaceutical Law Enforcement Officials.—*Chairman*, R. L. Swain, 2411 No. Charles St., Baltimore, Md.; *Secretary-Treasurer*, N. N. Ford, New State Office Building, Room G-18, Columbus, Ohio; *Delegate to the House of Delegates*, Fred Schaefer, Brooklyn, N. Y.

Plant Science Seminar.—*Chairman*, Frank H. Eby, 240 Powell Road, Springfield, Pa.; *Vice-Chairman*, L. K. Darbaker, 424 Franklin Ave., Wilkensburg, Pa.; *Secretary-Treasurer*, F. J. Bacon, Western Reserve University, Cleveland, Ohio; *Executive Committee*, C. E. F. Mollett, Montana; E. B. Fisher, Minnesota.

PHARMACY EXTENSION DEPARTMENT, PURDUE UNIVERSITY.

The fourth annual Druggists' Business Conference was held at Purdue University, March 20th. The occasion had added interest in the celebration of the semi-centennial of the school of pharmacy. Editor Jerry McQuade and Harry S. Noel delivered addresses. Al Fritz, of Indianapolis, discussed the present drug codes. Other speakers were Ray Whidden and Secretary Frank V. McCullough, who discussed legislation in Indiana.

The semi-centennial celebration was held following the conclusion of the Business Conference at which time the principal speaker was Dr. Edward Kremers of Wisconsin. The meeting closed with a banquet.

KANSAS PHARMACEUTICAL ASSOCIATION.

Kansas Pharmaceutical Association will hold its annual sessions in Salina, April 10th–12th. Among the speakers will be Dr. Frank Kirby, secretary of the Pharmacy Exhibit at the World's Fair in Chicago; his subject will be "Detailing for Prescriptions." As part of the program the Sayre Club will have a memorial meeting in honor of the late L. E. Sayre.

Election of officers of the Association is by mail ballot.

PENNSYLVANIA BOARD OF PHARMACY EXAMINATIONS.

Examination for applicants desiring registration as Pharmacist will be conducted in the Philadelphia College of Pharmacy, 43rd Street and Kingsessing Avenue, Philadelphia, and

the Pittsburgh College of Pharmacy, 1431 Boulevard of the Allies, Pittsburgh, on Thursday and Friday, April 5 and 6, 1934.

Assistant Pharmacist Examination—In the Philadelphia College of Pharmacy, 43rd Street and Kingsessing Avenue, Philadelphia, and the Pittsburgh College of Pharmacy, 1431 Boulevard of the Allies, on Saturday, April 7, 1934, 9:00 to 4:00 o'clock.

OKLAHOMA UNIVERSITY PHARMACEUTICAL ASSOCIATION.

The first annual convention of Oklahoma University Pharmaceutical Association was held March 9th in the Pharmacy Building, Norman, Okla. An interesting program, including all divisions of pharmacy was carried out: Scientific Section, Section on Practical Pharmacy and Dispensing, Section on Commercial Interests, Section on Historical Pharmacy. In each of these divisions instructive papers were read and discussed.

AMERICAN DRUG MANUFACTURERS' ASSOCIATION.

The American Drug Manufacturers' Association will hold its twenty-third annual convention at the Greenbrier, White Sulphur Springs, W. Va., April 16th to 19th. The scientific and biological sections have prepared an interesting program, including among other subjects concerning alkaloid and drug standards, analytical assay methods, chemical tests and standards, crude and milled drugs, digestive forms and glandular products, drug extracts, pharmaceutical investigations.

The chairman of the Committee on Alkaloid and Drug Standards, F. O. Taylor, has been studying some methods of tests now used in the Pharmacopœia, which are open to criticism in one way or another. The Biological Section has arranged a program which will have as a feature an address by Dr. George W. McCoy.

DISTRICT MEETINGS.

District No. 1, Board and College members, held its annual meeting at the Massachusetts College of Pharmacy, on March 14th–15th.

A very interesting and profitable meeting of the Boards of Pharmacy and the Colleges of Pharmacy in District No. 2, including New York, Pennsylvania, New Jersey, Delaware, District of Columbia and Maryland, was held at Hotel Emerson, March 12th to 13th. There was a very good representation from the several states. An address on "The Relation of Pharmacy to Public Health" was made by Dr. Huntington Williams, Commissioner of Health of Baltimore City. The Baltimore Branch of the A. Ph. A. took an active part in the meeting which will be reported with that of the Branch.

A general meeting of members of the bodies of District No. 7, comprising Georgia, Florida, Alabama, Mississippi, Louisiana, Porto Rico, was held March 26th–27th in St. Petersburg, Florida. The chairman for the Colleges was Wm. J. Husa; for the Boards, Charles H. Evans.

Among the questions discussed were the following: "Standardization of Experience," "Accuracy of Prescription Filling" from the teaching standpoint and from the enforcement standpoint, "Minimum Standards of Technical Equipment for Drug Stores," "Various Branches of Teaching and the Subjects to Be Taught," "The Nature of Board Examination Questions and Reciprocity." Legislation of various phases relating to the drug industry was discussed.

CONNECTICUT COLLEGE OF PHARMACY ESTABLISHES SCHOLARSHIPS.

Announcement has been made by the Connecticut College of Pharmacy that four scholarships, the total value of which is about $1000, will be awarded next September to graduates of high and secondary schools of Connecticut.

MID-WINTER MEETING, NEW JERSEY PHARMACEUTICAL ASSOCIATION.

The mid-winter meeting of New Jersey Pharmaceutical Association was held in Trenton, N. J., March 8th, at which time matters affecting legislation and concerned with the codes, were discussed.

The New Jersey Pharmaceutical Association and its Retail Drug Trade Alliance, have been working on a state code which has been presented to the legislature. There are pending in the legislature also bills affecting the practice of pharmacy and provision to investigate business methods and practice of chain and "cut rate" drug stores in New Jersey.

The New Jersey Board of Pharmacy will hold examinations for applicants for the Registered Pharmacist certificate at the State House New Jersey on April 19th.

NEW ENGLAND DRUG SHOW.

The New England Drug Show will be held at Mechanics Building in Boston during the week of April 2nd. At this time the annual spring conference of New England druggists will be held.

HISTORICAL EXHIBIT IN NEW BRUNSWICK HOSPITAL.

An interesting exhibit was arranged in St. Peter's Hospital, New Brunswick, N. J. The exhibit depicted the history of the institution by charts, photographs and statistical data.

A pathological and clinical laboratory was installed in 1920. In 1921 Dr. and Mrs. F. B. Kilmer founded a nurses' library of more than 2000 volumes in memory of their son, Joyce Kilmer, killed in the World War. Dr. Kilmer has been a member of the AMERICAN PHARMACEUTICAL ASSOCIATION for nearly a half century.

OLD APOTHECARY GLASSWARE.

Liebig's laboratory at Giessen, once internationally famous as a center of chemical instruction, has been converted into a museum housing exhibits illustrative and commemorative of the great scientist's many activities and interests. The pharmaceutical section is quite prominent. The museum is administered by a corporation, Gesellschaft Liebigmuseum, and its moving spirit is Prof. Robert Sommer of the medical school, who is largely responsible for the salvation of the old laboratory building for museum purposes, and to him also is due the credit for the untiring devotion entailed in collecting the interesting material on view.

The museum has a collection of glassware, reproductions typical of the Apothecary shop known to Liebig. Arrangements have been made for the reproductions by the Gesellschaft Liebigmuseum at Giesen. These bottles lend a charming and distinctive note to a pharmacy and may be obtained from the society mentioned.

LEGAL AND LEGISLATIVE.

CALIFORNIA FAIR TRADE ACT CONSTITUTIONAL.

Provision added by 1933 legislature, prohibiting "Unwholesome and Predatory Practices in the Merchandising of Goods," was upheld and defendant enjoined from selling below firm price fixed by distributor.

That section $1^1/_2$ of the California Fair Trade Act, added by the 1933 Legislature (Statutes of 1933, page 793) which forbids any person from wilfully and knowingly advertising, offering for sale or selling any commodity at less than the price stipulated in any contract entered into pursuant to the provisions of Section 1 of this Act, whether the person so advertising, offering for sale or selling is or is not a party to such contract, is unfair competition and is actionable at the suit of any person aggrieved—is constitutional, has been held by Judge Timothy I. Fitzpatrick of the Superior Court of the City and County of San Francisco, Department 8, in the case of Weco Products Co. of California *vs.* Sunset Cut Rate Drug Co., *et al.*, decided January 24, 1934.

NATIONAL RECOVERY ADMINISTRATION.

A committee of twelve members representing the distribution and consumers' service trade, similar in purpose to the two industrial committees named during the recent Code Authority Conference, was announced on March 14th by National Reconstruction Administrator, Hugh S. Johnson. This committee has been at work during the week and will advise the Administrator on various problems. The committee is headed by Rivers Peterson, *chairman* of National Retail Code Authority. The committee is composed as follows: (1) Retail, consisting of four members. The retail drug industry is represented by Secretary E. F. Kelly of the A. PH. A., who is also secretary of the National Retail Drug Code Authority. (2) Wholesale, composed of four members. The wholesale drug industry is represented by E. L. Newcomb, executive vice-president of the National Wholesale Druggists' Association. The consumers' service also has four members.

It is the intention of the committee to make a real contribution toward effecting all of the twelve points outlined in General Johnson's speech to the Code Authority Meeting.

THE AMENDED COPELAND BILL.

S. 2800:—Mr. Copeland of N. Y.: To prevent the manufacture, shipment and sale of adulterated or misbranded food, drink, drugs

and cosmetics, and to regulate traffic therein, etc., reported from committee on March 15th, the bill has been amended in a number of sections.

The labeling requirement for drugs used as a palliative for specific diseases has been changed to require that the nature of the palliative action of the drug rather than its palliative effect be shown on the label. The paragraph, providing that advertisements of drugs represented to have any effect in the treatment of a list of some forty diseases are presumed to be false, is striken out. For the purpose of consultation in formulating general administrative policies for the enforcement of the bill there is authority for the secretary to appoint advisory committees from the food, drug, cosmetic and advertising trades and from the public.

New sections added to paragraphs dealing with injunction proceedings would provide that as a means for avoiding multiplicity of libel for condemnation proceedings the federal district courts would have authority to restrain by injunction the institution of more than one seizure action against any product, (1) if the alleged violation is of misbranding only, (2) if all current shipments bear the same labeling, (3) if the alleged misbranding does not involve danger to health or gross deception, and (4) has not been the basis of a prior judgment in favor of the United States in any criminal prosecution for libel under the bill. The date when the bill is to become effective is made twelve months from its enactment into law instead of six months. Upon approval by the President, the Secretary of Agriculture is to designate foods having common or usual names and exempt them from the labeling provisions of the bill for a reasonable time to permit formulation, promulgation and application of definitions and standards of identity therefor.—Status: Reported by S. Com. on Commerce, 3–15–34.

According to press reports Arthur D. Whiteside, brought into NRA by General Johnson as administrator, has vacated his Washington quarters and returned to New York to resume his place as president of Dun & Bradstreet.

BOOK NOTICES AND REVIEWS.

The Chemical Formulary distributed by the Chemical Formulary Company, Bush Terminal Building No. 5, Brooklyn, N. Y. 600 pages. Price $6.00. The Board of Editors consists of about sixty contributors.

The Formulary contains methods for making varieties of face and skin creams, toilet preparations including lotions, shampoos, hair preparations, tooth powders and pastes, perfumes, bleaches, deodorants, etc. Other lists include anti-freezes, adhesives, beverages, blacking, cleaners, colors, crayons, driers, drycleaning soap, dyes, embalming fluid, emulsions, enamel, explosives, extracts, fillers, fire-proofings, foams, food specialties, fuel, glazes, glue, incense, insecticides, ink, lacquer, latex, leather, liniments, liquor, lubricants, moth exterminators, mildew-proofing, mouthwash, paint, pigments, plastics, plating polish, preservatives, rat-poison, rubber goods, rust-proofing, shoe cleaners, soaps, solvents, styptics, varnish, viscose, waterproofing, wax, synthetic wax polish, weed killer, wood filler, etc.

The publishers state that many of the formulas are used commercially, others are taken from patent specifications, publications and other sources, with the end in view of supplying dependable information. The value of formulas depends largely on whether practical and satisfactory application has been made of them; how far this has been done the reviewer is not in position to say. There is lack of uniformity in the publication of formulas, in abbreviations, capitalizing, in giving quantities, etc. This may not detract from the value of the formulas but it is noticeable, thus, under "Removing Stains—Chromic Compounds, Chromates: Sod. Bisulphite or Sod. Hyposulphite and dilute sulphuric acid." Lead Compounds:—"Stain with Tinc. Iodine; dry and dissolve with concentrated pot. iodide solution."

Quantities are given in different weights and measures, in parts, in percentages and without designation; such variations occur on the same page. A heading reads "Stone, Artificial," the one following, "Synthetic Stone." In a formula there are the following abbreviations: "compn." for composition; "prepd." for prepared. "HCl," the strength is not given. As heretofore stated, these defects may have no bearing on the value of a formula. Some of the formulas are indefinite, but no attempt has been made to check up on ingredients and quantities and the resulting product; it is assumed the publishers have endeavored to present formulas that are reliable. However, in the opinion of the writer, the value of "The Chemical Formulary" is not enhanced by the inclusion in some formulas of certain advertised specialties, without naming the constituents.